The Physiologist

Henry Pickering Bowditch

First President
American Physiological Society

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THE AMERICAN PHYSIOLOGICAL SOCIETY

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The seal at the top of this page was designed by William F. Hamilton and has been adopted by the Council as an official emblem of the Society.

Editor's Page

This is the first issue of a new trial organ, mainly for the membership but it is hoped will be of interest to others. Four issues a year will be published, November, February, May and August. The November issue each year will contain the abstracts of the papers presented at the Fall Meeting. The other three issues will be less bulky and contain a variety of material we hope will be of interest to all physiologists. The February 1958 issue will contain: list of persons nominated for membership at the 1957 Fall Meeting; proposal for associate membership; Bowditch lecture by Bodil Schmidt-Nielsen: President's message; section on instruments; an article on education; various announcements and special items.

The editor invites members to submit announcements of events of interest to physiologists; news items about physiologists or physiology; special articles not suitable for research journal publication but of timely interest to physiologists; and any suggestions to make the new journal of interest and use to physiologists. Address all communications to 9650 Wisconsin Avenue, Washington 14, D. C.

IN RETROSPECT

The American Physiological Society was founded at a meeting held on December 30, 1887 in the physiological laboratory of the College of Physicians and Surgeons, 437 West 59th Street, New York City. A self-appointed committee consisting of Silas Weir Mitchell, a practicing physician of Walnut Street, Philadelphia; Henry Newell Martin, Professor of Biology at Johns Hopkins University; and Henry Pickering Bowditch, Professor of Physiology at Harvard Medical School, was mainly responsible for organizing the Society. There were 28 charter members and Dr. Bowditch was the first elected president.

William Townsend Porter, of Harvard Medical School, was the person most responsible for founding the Society's first official organ, *The American Journal of Physiology*, since he was its first editor and took full financial responsibility for the Journal. The Society did not own the Journal until 1914 when Donald Russell Hooker of Johns Hopkins was appointed Managing Editor. Even though *The American Journal of Physiology* had a board of editors it was not until 1933 that the Society appointed a Board of Publication Trustees and gave it full authority in the control and detailed management of its journals.

By 1920 the Society saw the need and demand for a second

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journal, one to be devoted to exhaustive reviews of reliable scientific topical data. As a result of the work of Dr. William H. Howell, Dr. Hooker, Dr. Anton J. Carlson and others the journal *Physiological Reviews*, was launched in 1921. Dr. Howell was appointed Chairman of the Editorial Board and served until 1932 when Dr. Carlson was appointed. Dr. Hooker served as Managing Editor for both journals until his death in 1946. Dr. Milton O. Lee was appointed Managing Editor of the Society's journals in 1947.

There was a growing demand for still another journal for reporting research emphasizing man's relation to his environment and the adaptations of his physiological mechanisms to the many and varied stresses imposed upon him. After much discussion and the broadening of the scope of the proposed journal to include various aspects of applied physiology, the *Journal of Applied Physiology* was started in 1948.

By 1948 the membership of the Society had grown considerably and a smaller percentage of the total membership was attending Society Business Meetings. It was felt that the membership should be informed of actions taken by Council and the Society so the Executive Secretary sent a sheet titled "General Information and Summary of Society Business" to all members with the announcement of the Spring Meeting. This grew into a Semi-Annual Notice, then the News Letter. In 1953 it became the President's News Letter issued twice a year. In 1956 the Board of Publication Trustees, feeling that the President's News Letter filled a definite need, offered to subsidize, on a two-year trial basis, a new house organ type of journal to replace the President's News Letter. The new organ was to be published quarterly and in addition to carrying the type of material previously contained in the President's News Letter was to contain the abstracts of papers presented at the Fall Meetings, the Past President's Address, education articles, news items, etc. The Council approved and thus the birth of *THE PHYSIOLOGIST* with its first issue in November 1957.

SPRING MEETING

The 71st Annual Spring Meeting of the American Physiological Society will be held in Philadelphia, April 13-18, 1958 in association with the other constituent societies of the Federation. Abstracts must be mailed to arrive at the central office, 9650 Wisconsin Avenue, Washington 14, D. C., not later than 1 January 1958. Each abstract must be submitted on a special form, limited to 250 words and carry the signature of a member of the Society. Details concerning the preparation of abstracts are being mailed to the members along with hotel reservation forms, reprint order forms, applications for exhibit space, suggestions to speakers and other announcements.

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PROCEEDINGS

Fall Meeting, September 3-6, 1957

THE HUMAN SIDE OF THE PHYSIOLOGIST, PREJUDICE AND POETRY

(Extracts from the more serious part of the address of the Past President, Alan C. Burton, after the annual dinner of the Society in Iowa City, September 5, 1957)

Since I am known to hold the title of Professor of Biophysics, I might be expected, in a serious address, to supply a definition of biophysics. The number of different definitions that have already been given bears a striking relation to the number of people who call themselves "biophysicists." The only reliable definition is, therefore, that "biophysics is what the biophysicists do." However, with the gift of a captive audience before me, I would probably seize the opportunity to say how, in my view, biophysics is a branch of physiology, in the old sense of "physiology," meaning the study of the normal functioning of living things; a branch similar in status to physiological chemistry. If my chief interest is in living things, rather than in the inanimate, and if, when I see the workings of a living cell or organism, I am interested to find out the physical laws that are operating—then I am a fundamental biophysicist, in the tradition of Borelli and of Helmholtz. In addition, of course, to be worthy of the name of biophysicist, I should have adequate training and ability in physics and mathematics to enable me to discover and understand the physics of living things. After all, in modern physiological research, to contribute greatly, a man has to have some special aptitudes in either chemistry, or in physics and mathematics—both as regards the tools of research—and, more importantly, in the tools of thinking about the results of research. I am not at all belittling the role of the "integrative physiologist," for one of the greatest mistakes a physical scientist approaching the study of life could make would be to suppose that the physical and chemical constitution, and the laws of physics and chemistry operating upon individual cells, suffice to explain the functioning of organisms. Over the physiological chemist, and the biophysicist, must stand the "integrative physiologist" who looks at the whole and the connections between its various parts, and who can utilize the knowledge of mechanisms gained by the biophysicist and biochemist to complete his own study of biological organization.

I think, in a serious philosophical address, I'd be inclined to spend most of my time discussing the curious "schizophrenia" of the basic scientist. I would discuss how the philosophers of science, like Whitehead and Russell, agree that the essence of science is the removal of all passion, prejudice or pressure of preconceived ideas in a scientific judgment in the face of the "facts." Science is, at its core, not concerned with what "must be," and far less with what "ought to be" (this is the realm of morals and ethics), but with "what is." The true scientist is he who, in the ultimate conflict of even the best of logical systems, and of prediction from what is already known, in a conflict with the results of experiments, acknowledges the primacy of the evidence. In this sense, science is almost anti-rational, anti-intellectual; and the 19th century identification of "science" and "reason" has led many astray. At the trial of Galileo, it was the

inquisitors that represented "rationalism," and it was Galileo who muttered under his breath "And yet it does move."

I am confident that most of us would pass the test, certainly in our own field of science, and that our ultimate allegiance is to the results of experiment and observation. The facts must mold the theories, not the theories the facts. I am not so sure that we remember this, when it comes to reports of phenomena outside our own immediate field. Does the usual attitude of scientists to reports of, say, paranormal phenomena, for example, extrasensory perception, reflect the true scientific spirit? Or when a Paul Weiss reports experimental results that challenge the basis of the localization neurone theory, do we just shrug our shoulders and ignore the evidence? The true scientist says "Let's examine the evidence and, if it is reproducible we must patch up our preconceived notions and theories, or discard them and begin with new ones."

I am most critical of my biologist friends in this matter. It seems to me that they have allowed what is a most useful working hypothesis, in a limited field of the whole of biology, to become "dogma," in their worship of the principle of natural selection as the only and sufficient operator in evolution. If they have done this, they no longer can act as true scientists when examining evidence that might not fit into this frame of concepts. If you do not believe me, try telling a biologist that, impartially judged along with other accepted theories of science, such as the theory of relativity, it seems to you that the theory of natural selection has a very uncertain, hypothetical status, and watch his reaction. I'll bet you that he gets red in the face. This is "religion," not "science" with him.

The physicists have learned their lesson from their past. They remember how, once, "it must be" that the velocity of light would alter according to whether the earth was approaching or receding from the sun (and yet it did not so alter), how mass must be invariant, (and yet the atom bomb), how radiation must be accumulated in the longer wavelengths (and yet the facts demanded the quantum theory). In this respect the physicists are better scientists than the biologists, for whom some smashing of their icons would be most salutary. "There are more things in heaven and earth, Horatio, than are dreamed of in your philosophy."

Yet here's the paradox. In my experience, the really creative research scientists are full of "passion" for their preconceived ideas; they know just what they want to find, what they want to prove in the experiments they perform. And why not? If we don't know what we are looking for, it is very improbable (thought it happens now and then) that we will find anything worth while. As Chesterton once said: "What is the use of redoubling our efforts, if we have forgotten our goal?" I have met a few who advised young research workers to "just collect the facts, without any idea of what you expect to find, far less what you want to find, and then analyse them." I seriously doubt if this method of research ever made many contributions to science. For one thing, it would be so dull that the necessary alertness, as Francis Bacon put it: "to be quick to catch the resemblances of things," would probably be lacking. Prejudice, preconceived ideas and systems of ideas, enthusiasm for his own point of view—these are the working attributes of a productive scientist. Yet he must unerringly, in the crisis of a contradiction, by the data, of all he has cherished in theory or prediction, renounce Love for Duty (like the hero of a Victorian novel).

In a serious speech, I would pass on to dicuss the fascinating human traits of the scientist, who yet is devoted to cold, inhuman science. The inconsistency has been beautifully expressed in verses I found in the columns of The New Yorker, April 1953, by May Sarton, who is, I am told, herself a daughter of a great writer of the history and philosophy of science.

DIALOGUE*

The teacher of logic said, "Reason."

The poet said, "Passion."

"Without logic, we muddle
And fail," said the teacher
Of reason.

The poet said, "Fiddle!
What about Nature?"

"Has Nature no plan,
You poor, fuddled creature?
You're a rational man,
Not an ape or an angel."

The poet said, "Nonsense!
I'm an angel, an ape,
And a creature of sense,
Not a brain in a box
That a mere jackanapes
With logic unlocks.
I'm total. I'm human,
It's you who are not."

"You sound like a woman."

The poet said, "Rot!
You're just a machine.
You can't write a poem.
You can't make a dream."

But the logical man
Said, "I'll stick to my reason."

(He said it with passion.)

Why is it that there has been so little poetry written about science and the scientist? To me, there is everything in the life and dedication of the scientist to inspire it. There is the sense of community and interdependence of all scientists, the knowledge of our heritage, of how our efforts may make complete a beautiful structure, to which we have merely added the final brick. One summer, on vacation in our lovely and rocky Ontario Lake District, I tried to express it thus.

A miracle, that hemlock, on the naked rock
Can live and grow.
Its roots are based on leaves that fell
So many lives ago.
I know more than Newton, can argue with Pasteur,
And yet with deference;
My roots are based on libraried stores
Of reference on reference.

My mind is not my own, a pseudopod
Of classic minds.
Here, and in Elysium
Of one Mind, one single Mind of Science,
One pulsing, huge, coordinate, Syncytium.

*1953 The New Yorker Magazine, Inc.; included in the collection In Time Like Air (Rinehart and Co.).

Then in the romantic "adventures of the mind" that a career in science can offer, particularly in biological science, there is surely material for the poet. We do not have to make a completely new discovery, or win the Nobel prize, to experience the thrill of understanding, even where many may have understood before. The joy of enlightenment, of recognizing a familiar, or a new pattern in nature, the ghostly light shining in the darkness of ignorance. . .these are the rewards of being a research physiologist. I suppose the experience is different to every one of us; the details of our adventures of the mind are varied. This is how it feels to me, rather like the progress of a river from its source to the Great Lakes.

DISCOVERY

Little rivulets of thought
Erode the broad surface of the problem posed,
Idle, wandering and aimless rills
Like garden freshets after heavy rain.

And now the streams have quickened, coalesced,
To eddy round the hillock of a doubt,
Find well-worn channels, ditches study-dug,
And flow with purpose in a common trend.

Ideas break surface with a salmon-splash,
While from the deep,
Wise intuition adds its hidden flow,
A rhythmic pulse is growing, surge on surge,
Insistent logic in bolero-time.

At last the turgid waters will not stay—
Glide swiftly through the gorges of analogy,
Go leaping down the rapids of hypothesis,
and break
Into a quiet flood of certainty.

Then there is the motivation of the scientist, which is so far from what the public is inclined to think, namely that our mainspring of motive is to make "better things for better living, through physiology." Of course we are all delighted if our researches produce something immediately useful, say in medicine, but if this be our chief motivation, we'll miss the best of physiology as well as of fun. Our motivation is really very similar to that of the artist, and has little of the spirit of the engineer. It is a matter of inner compulsion. As Bacon put it, "We are endowed by nature with the desire to seek."

You have all heard of the story about Michael Faraday, and his reply to the question after one of his public lectures, "What use is it?" He replied, "What is the use of a newborn baby?" Only recently did I realize that this is really subversive propaganda directed against scientists, spread no doubt by infiltrating engineers. So I wrote the following (and I have been so carried away with the chance to spout my own verse to an audience, that I have forgotten this is only an after-dinner speech, so this must be the end. . .).

APOLOGY FOR SCIENCE

Mr. Michael Faraday, of the Royal Institution,
Gave public lectures every month, complete with demonstrations,
With rods of ebonite and sealing wax
And fur of cats, and Leyden jars
And magnets swinging on a thread
And piles of copper plates, and pumps and flasks
And all festooned with mathematics.

Earnest students, and the patron rich,
Idle ladies, and the sheltering bum,
And even now and then a Royalty
Would fill the floor and galleries,
Gossiped, yawned, took tidy notes
Or slept.

A smug old lady of the lecture-loving kind,
Joined the admiring after-questioners and said:
"Mr. Faraday, all this is very fine, most interesting
And oh, so very clever.
But will you tell me, please,
What use it is?"

The scientist replied:
"Madam, will you tell me —
What is the use of a new-born child?"

And ever since, when people hear
Of studies on metabolism of the ant,
Of chromosomes, contractile vacuoles, chlorophyll,
The sex-life of the beetle, resonance in molecules,
Or photo-synthesis,
They tell this tale, and usually explain
That babies grow to Presidents, or Henry Fords, or Edisons,
Or anyway to carry mail, or dig, or sweep —
And who can tell?

Of course it's difficult to see how this applies
To History and Classics,
Research in Anthropology or Cosmic Evolution
And other really useless studies.
But here we recognize
That the really cultured social hide supports,
Like fleas upon contented dogs,
Permitted parasites.

What a travesty in this, on Faraday and Science!
Are babies born, conceived for usefulness,
Planned as prospective workers, raised like stock?
Or is it Love, or innate Constitution?
Must not the sons of men, because they are,
Create and procreate?
And madam . . . have you never met
The proud new parent, driven by the urge to tell
Each precious infant detail?

Ah, no . . . it is the nature of the beast
That maggots breed, that dogs must bark
And scientists investigate.
The faith of Faraday endures . . .
There is a Pattern, by whatever loom,
And men by search must find it.

ABSTRACTS OF PAPERS READ

An asterisk following an author's name denotes 'by invitation'

QUANTITATIVE BIO-ASSAY OF THE OXYTOXIC FACTOR IN PLASMA. H.P.K. Agersborg, Jr. and J. D. Meyers (intr. by G. B. Spurr). Inst. of Clin. Investigation, Univ. of Tennessee Med. Units, Memphis.

No previously reported bio-assay method has been able to quantitate the normal peripheral blood levels of the oxytoxic factor in an acceptable manner. This method employs the standard isolated rat uterine horn, a tissue bath, muscle lever and kymograph but differs from the usual in that the entire uterine activity is recorded as a contraction curve area. The inherent activity of the uterus made necessary the measurement of a control area immediately before each test. The difference between the control and test areas was taken as the response to the injected agent. Serial dilutions of aqueous pitocin have indicated that 4×10^{-5} units is the minimal bath concentration always capable of eliciting a uterine response. It was further found that from 4×10^{-5} to 16×10^{-5} units the rat uterus responds in a straight line, does-linked manner with the slope of this line varying for each uterine horn. Using a single lot of pitocin as a constant reference, it was possible to plot the response to 4×10^{-5} and 8×10^{-5} units, connect these points and quantitate the area response of 1 ml of plasma directly in oxytoxic equivalents. This method is capable of differentiating 4×10^{-5} units of aqueous pitocin in plasma with a mean recovery of 100%.

RESERPINE EFFECTS IN THE MOUSE AND THE ADRENAL. Paul Albrecht*, Franz Halberg and John J. Bittner*. Univ. of Minnesota Med. School, and Cambridge State School and Hosp., Minneapolis.

Graded doses of reserpine were administered to intact, sham-operated and adrenalectomized male B_1 mice. In the intact mouse, 250 μg/kg was the minimal eosinopenic dose, in tests carried out during the ascending phase of eosinophil rhythm (J. Clin. Endocrinol. 12: 932, 1952). In the state of adrenal insufficiency, eosinopenia was not obtained in response to that dose, but a marked hypothermic effect preceded death by several hours. Moreover, in adrenal insufficiency, doses of reserpine smaller than the minimal eosinopenic dose were extremely toxic (cf. Gaunt et al. Ann. New York Acad. Sc. 59: 22, 1954). Thus, at 7 hr post-injection, 80% of adrenalectomized mice given 125 μg/kg of reserpine were dead, as compared to 5% death of the adrenalectomized controls given saline. The adrenal glands appear to be an essential link in the mediation of the eosinopenic effect of reserpine as studied herein. These studies also emphasize the potential dangers of reserpine administration in states of adrenal insufficiency.

DEVICE FOR RAPID FRACTIONATION OF PARTICULATE SYSTEMS BY GRADIENT DIFFERENTIAL CENTRIFUGATION. Joseph F. Albright* and Norman G. Anderson. Biology Div., Oak Ridge Natl. Lab., Oak Ridge, Tenn.

Although the centrifugal separation of particulate systems into components of relatively uniform size and density is greatly improved by the use of continuous density gradients, the technique is seldom used. The time required for the establishment of satisfactory gradients is prohibitively long, and the volume of starting material that can be effectively fractionated is small. These difficulties are eliminated by a distribution head designed for use in conjunction with a six-place swinging bucket head in the International Equipment Company's model PR-2 centrifuge. The circular, stainless steel distribution head is divided into 6 equally spaced, radially oriented concavities. With the centrifuge running, the cups are swung to the horizontal position; and the bottom of each concavity in the distribution head is connected with the bottom of a 200-ml pyrex bottle through a

conduit tube. A brei or suspension of particles is poured into the distribution head, followed by the least-dense cut of liquid from a gradient engine and then by progressively denser liquid. Within 10 min identical density gradients are established in the 6 bottles. Mixing is prevented by the centrifugal force. Rat liver mitochondria were isolated in sucrose gradients. Microscopic examination of this fraction revealed the complete absence of contaminating nuclei and the uniformity of the fraction with respect to particle size. The pellet resulting from high-speed centrifugation of these mitochondria was devoid of a "fluffy" layer. The fraction contained 0.04 γ of nitrogen, 0.21 γ of protein and 0.01 γ of ribonucleoprotein per million mitochondria.

OXYGEN DEPENDENCE OF ATP INDUCED CONTRACTION OF GLYCERATED PSOAS MUSCLE. Norman Alpert and Iris Maggiolo Barbato (intr. by Raymond C. Ingraham). Dept. of Physiology, Univ. of Illinois College of Medicine, Chicago.

ATP induced contraction of glycerol treated psoas fibers was studied in oxygen, room air, argon and nitrogen. In each of the experiments the extent of contraction was studied at a final molar ATP concentration of 4.10^{-3}, 1.10^{-3}, 5.10^{-4}, and 5.10^{-5}. Potassium chloride and magnesium chloride were maintained constant for all of the experiments at a final molar concentration of .1 and .001 respectively. Phosphate buffer was used to maintain the incubating medium at pH 7.0. At the highest concentration of ATP glycerated fibers in oxygen shortened from 4.00 cm - .75 cm or 81%. This is the maximal contraction of the fiber. At a final molar ATP concentration of 5.10^{-5} the percent of maximal contraction in oxygen, room air, argon and nitrogen was 56, 44, 38 and 30; at an ATP concentration of 5.10^{-4}M the percent of maximal contraction was 77,64, 55 and 53; at an ATP concentration of 1.10^{-3}M the percent contraction was 80, 68, 59 and 62; at an ATP concentration of 4.10^{-3} the percent contraction was 100, 77, 65 and 68.

ACTION OF TRICYCLAMOL SULFATE ON GASTRIC SECRETION OF POUCHED DOGS. R. S. Alphin* and T. M. Lin. Lilly Research Lab., Indianapolis, Ind.

A study was made of the effect of Tricyclamol sulfate on the acid secretion of pouch dogs following stimulation by a standard test meal or histamine or insulin. One to two mg equivalents of the free base of Tricyclamol per kg were given orally 1 hr before feeding a test meal. After feeding a test meal of 100 or 200 gm of Pard, the free hydrochloric acid secretion was completely inhibited an average of 1-2 hr at 1 mg/kg, and 3-4 hr at 1.5 mg/kg of body weight. The volume secretion decreased by 50% within the 4-hr period following a 400-gm test meal, but complete inhibition of free acid secretion was not seen. A 30-μg dose of histamine sulfate given subcutaneously at 10-min intervals was selected as a test dose for gastric response in 5 denervated pouch dogs. One mg/kg of Tricyclamol significantly reduced the volume and total acid output but had no effect on acid concentration. Two innervated pouch dogs were tested for gastric response to 10 units of insulin. One mg/kg of Tricyclamol decreased the volume by 60% and the acid output by 30%, whereas 2 mg/kg of Tricyclamol completely abolished free acid secretion for 1-3 hr. It is concluded that Tricyclamol at a dose equivalent to the human dose reduced the meal- and insulin-stimulated secretion of dogs. It had only a volume reducing effect on histamine-stimulated secretion.

FACTORS AFFECTING OSMOTIC ACTIVITY OF BOILED TISSUES. Johannes W. Th. Appelboom*, Walter Neil Scott* and William A. Brodsky. Depts. of Physiology and Chemistry, Univ. of Louisville, Ky.

A previous report showed that boiled tissue extracts were closely isotonic to plasma. Control experiments on diffusion equilibrium, CO_2-loss with boiling, and change in activity coefficient with dilution confirmed that such extracts were isotonic with serum. Remaining questions concerned the effects of heat and

dilution on changes in colligative properties of tissue proteins. Present data indicate that: 1) boiling does not change the freezing point depression of hypertonic tissue homogenates; 2) freezing and crushing of boiled isotonic tissues in a hydraulic press induces no significant increase in their osmotic activity; 3) freezing and thawing of boiled isotonic tissues does not increase their osmotic activity; 4) homogenizing of boiled isotonic tissues in a glass homogenizer does not increase their osmotic activity. Microscopy showed cell destruction in the homogenates. One might infer that boiling renders tissue isotonic by rendering isolated regions impermeable to osmotically active solutes. However, destruction of cell barriers fails to release any solutes, which might have been "trapped" in some way by the boiling procedure. It is concluded that boiled tissue extract is isotonic to plasma even after freezing, crushing and homogenization. A question remaining would be to distinguish the effect of freezing and crushing on living proteins from that on heat coagulated proteins.

HEMODYNAMIC CHANGES IN ADRENALECTOMIZED DOG INFUSED WITH PLASMA. Carleton H. Baker (intr. by John W. Remington). Dept. of Physiology, Med. College of Georgia, Augusta.

Adrenalectomized and adrenalectomized-splenectomized dogs, maintained for a minimum of 2 wk on DCA therapy, anesthetized (morphine-Nembutal), were administered 120 cc of sterile normal dog plasma i.v. at a rate of 4 cc/min. Aortic pressure was recorded optically and the cardiac output calculated from the pulse contours. The electrocardiogram was recorded. Whole blood and plasma specific gravities were obtained and the hematocrit determined. During the infusion period the blood pressure rose moderately with some widening of the pulse pressure. There was little change in heart rate or central venous pressure, and the cardiac output showed no clear rise. However, there was some increase in the total peripheral resistance as well as a fall in hematocrit. Following the infusion there was a steady fall in blood pressure and in cardiac output (1-2 hr). Some dogs showed the decline starting while the infusion was in progress. The heart rate either remained essentially constant or accelerated. Sometime before death, a bradycardia developed. The peripheral resistance dropped significantly during the post-infusion period. The central venous pressure decreased at the same time and remained low until the death of the animal. A failure of venous return seems indicated. The plasma specific gravities decreased slightly and the venous hematocrit increased somewhat even in the splenectomized animals. Benadryl pretreatment delayed or eliminated the arterial pressure fall and the hemoconcentration. (Supported by grants from USPHS (No. H-240) and Life Insurance Medical Research Fund.)

GRADIENT OF ABSORPTIVE ACTIVITY FOR BILE SALT ALONG THE SMALL INTESTINE OF THE RAT. R. David Baker and Gordon W. Searle (intr. by J. D. Thomson). Dept. of Physiology, College of Medicine, State Univ. of Iowa, Iowa City.

Intestinal absorptive activities for conjugated cholates defined as the mg of cholate absorbed per cm length of intestine per hr, were determined at various levels of rat small intestine using isolated segments of intestine in vivo. Seventeen, adult, male, albino rats were used, each animal providing one segment of intestine. The segments ranged from 7 - 19 cm in length. The intralumenal hydrostatic pressure in each intestinal segment was maintained between 3.5 and 5 cm of water throughout the hour-long absorption period. Extract of Ox Bile, U.S.P. (Wilson), was used as the source of bile salt. Absorptive activity was seen to increase as the mean distance of the segment from the pylorus increased. This relationship between absorptive activity (Q) and mean distance (m) appeared to be exponential and to be represented satisfactorily by the equation: $Q = 0.459 \times 10^{0.00740\ m}$. The absorptive activity gradient, given by dQ/dm, was, therefore, $0.00780 \times 10^{0.00740\ m}$ $mg/hr/cm^2$. This apparently inherent property of the intestine may have fundamental physiological importance in the process of fat absorption. This work confirms and extends the work of Frolicher (Biochem. Ztschr. 283: 273, 1936). (Supported by a grant from the USPHS.)

FAST VITAL CAPACITY CURVES AND MAXIMUM BREATHING CAPACITY PREDICTION. R. G. Bartlett, Jr., H. F. Brubach* and H. Specht. Lab. of Physical Biology, Natl. Inst. of Arthritis and Metabolic Diseases, Bethesda, Md.

The maximum breathing capacity (MBC) predicted from the fast vital capacity (FVC) curves increases with increasing breathing rates. Experimentally determined curves, however, show that the MBC increases only to a given breathing rate (about 100 breaths/min with low airway resistance and 40 breaths/min with high airway resistance) after which it decreases. This discrepancy between the predicted and observed MBC-breathing rate curves is most likely a result of a volume deficit resulting from time lost, as far as air movement is concerned, in flow reversals during breathing. Comparison of predicted and observed MBC at several different airway resistance levels is shown and the volume deficit per breath is estimated. Inspiratory and expiratory FVC curves have also been determined with various increased airway resistances. MBC-breathing rate curves were determined from these FVC curves. These are compared with experimentally determined curves at the same resistance levels. A similar volume deficit, presumably due to flow reversal, was again noted. The discrepancy became marked at breathing rates higher than the rate at which the peak MBC occurred (ca. 40 breaths/min) and was very great above 100 breaths/min (where peak observed MBC at low resistance levels occurs). It follows, then, that in individuals with constrictive or fibrotic respiratory lesions the prediction error may be very large if MBC is estimated at the usual breathing rate for peak MBC. It is small, however, if estimated at the breathing rate at which the peak observed MBC actually occurs.

INFLUENCE OF CHLORPROMAZINE ON CEREBRAL BLOOD FLOW AND ITS PROTECTIVE ACTION IN O_2 AT HIGH PRESSURE. John W. Bean and Herbert Wagemaker*. Dept. of Physiology, Univ. of Michigan, Ann Arbor.

Blood flow through the internal carotid artery of heparinized dogs anesthetized with Na-pentabarbital was followed continuously by thermopile method, all other branches of the common carotid artery and sinus, and all interconnections between the internal and external carotid artery having been previously occluded. Chlorpromazine (Thorazine (Smith, Kline and French) in doses of 1.2, 0.6 and 0.3 mg in 1/2 and 1/4 cc of 0.9% NaCl solution) administered by close intra-arterial injection evoked an almost immediate and frequently well sustained increase in cerebral blood flow either without any concurrent effect on systemic blood pressure or with a later gradual decrease. Intravenous administration of larger doses (5.5 mg) usually caused a gradual decrease in systemic blood pressure and some slight decrease of blood flow, but intra-arterial injection of the smaller doses still evoked a well pronounced increase in cerebral blood flow without any attendant alteration in blood pressure. The data indicate that close intra-arterial injection of chlorpromazine has an immediate vasodilatatory action on cerebral vessels whereby it increases cerebral blood flow. The immediacy of this flow increase and the fact that it occurs in the absence of concurrent changes in systemic blood pressure, in hypotensive states, or with a falling systemic blood pressure bespeaks the potency of this vasodilatatory action and its independence of changes in systemic blood pressure. It appears, that at least the early protective action of chlorpromazine against the toxicity of O_2 at high pressure involves more than a simple reduction of cerebral blood flow. (Supported in part by USPHS Grant H-1646.)

INDUCED MECHANICAL AND ELECTRICAL RESPONSES OF INTACT THENAR MUSCLES OF PATIENTS WITH MUSCULAR DYSTROPHY. Sibyl Beckett*, Eleanor Bendler* and Stella Y. Botelho. Dept. of Physiology and Pharmacology, Grad. School of Medicine, Univ. of Pennsylvania, Philadelphia.

Simultaneous electrical activity and isometric tension were recorded from the thenar muscles of 9 male (aged 4-25 yr) and 1 female (aged 14 yr) patients with muscular dystrophy when their ulnar nerves were stimulated with supramaximal to threshold single shocks, trains of supramaximal shocks (3/sec and

30/sec) and supramaximal paired stimuli with different conditioning-test shock intervals. The overall mean values, compared with values obtained from normal subjects, showed: decrease in amplitude and area of the negative phase of the single supramaximal action potential but an increase in the duration; decrease in initial tension and increase in maximum developed tension, 3/4 relaxation period and latent period of contraction of single supramaximal twitches; increase in the 3/4 relaxation period and residual tension period with tetanus (30/sec); increase in the potentiation of the second of paired responses and increase in the refractory period range. In addition, unlike normal subjects, the dystrophics showed a progressive decrease in maximum developed tension of successive single twitches (obtained with trains of supramaximal stimuli at 3/sec for 2 sec) without similar changes in the area of the accompanying action potentials. The mechanical responses to single and paired stimuli were similar to those reported in genetic dystrophic mice by Brust and Sandow (Fed. Proc. 16:17, 1957). Larger variations in values were obtained among the dystrophics than among the normals.

ORIGIN OF ELECTROMOTIVE FORCE OF THE ELECTRIC ORGAN. Reinhard H. Beutner. Med. Research Lab., Des Moines Still College, Des Moines, Iowa.

The electric organ of Electrophorus electricus produces up to 500 volts. Its discharges are the result of a constant electromotive force and a variable resistance. In the resting conditions the organ's resistance is high, so as to prevent discharge, but drops on stimulation, allowing an intensive current to pass. The organ's constant electromotive force is produced by an alternate arrangement of basophilic and acidophilic layers, according to K. H. Meyer (Biochem. Ztschr. 277: 39, 1931). To quote: "a single columnar unit of the organ is built of lamellae which alternately stain with acidic and basic dyes, respectively." Artificial systems can be set up of alternating "basophilic" and acidophilic layers. A "basophilic" layer can be obtained by adding to olive oil, or another lipid, higher fatty acids like oleic acid. This oil mixture will take up and hold basic dyes like methylene blue ("basophilic stainability"). Another batch of olive oil is rendered "acidophilic" by addition of a water-insoluble base or amine, as e.g. di-amylamine or an alkaloid. The basophilic and the acidophilic oils are then used to set up artificial battery systems as e.g. - saline | acidophilic oil | basophilic oil | saline +. Methods of measuring the electromotive force of such battery systems have been described (Beutner, "Bioelectricity" in Handbook of Biophysics, 1944). The emf is found to be 0.14 volt, the positive pole being on the side of the basophilic layer. The electric organ contains 3000-5000 electrical units arranged in series, each of these producing 0.14 volt, so that a voltage of 500 results. (Supported by a grant from the Natl. Heart Inst., USPHS.)

PYRAMIDAL STIMULATION BY MEANS OF DEPTH ELECTRODES IN MAN. Reginald G. Bickford, E. H. Lambert and H. N. A. MacDonald*. Lab. of Electroencephalography, Mayo Fndn., Rochester, Minn.

While investigating the location of deep epileptogenic lesions in patients with a view to subsequent therapeutic excision, it is frequently possible to study pyramidal function resulting from stimulation in the zone surrounding the scar lesion. Such observations have been made in 3 patients. Stimulation (1-10 volts, 0.3 msec, 1/sec monophasic pulses) is applied through 39 gauge stainless steel wires, bared for 1 mm and separated by 1 cm which have been implanted through burr holes. Single and paired pyramidal stimuli have been employed and the interaction between a pyramidal volley and one induced by stimulation of a corresponding afferent nerve (e.g. tibial or ulnar) has been investigated. Pyramidal stimuli consisting of single pulses produced single twitches of contralateral muscles. At threshold a few fibers within a muscle (e.g. platysma) may respond. Increase of stimulus voltage produced more widespread movement, often complex and apparently unphysiologic (involving agonists and antagonists). Voluntary contraction markedly accentuates the pyramidal twitch and reveals an inhibition of voluntary tone following the contraction. The latency of the pyramidal induced twitch in the leg (calf muscle) is 24 msec. In the presence of voluntary

contraction there is a silent period (lasting approximately 70 msec). After the onset of the response to pyramidal stimulation there was a facilitation of reflex responses to stimulation of the tibial nerve ("H" reflex of calf muscle) which was maximal at 10 msec and lasted approximately 70 msec. The amplitude of the pyramidal induced twitch is reduced during sleep and anesthesia (barbiturate).

EFFECT OF DOUBLING AND QUADRUPLING INDICATOR DOSE ON DILUTION CURVES. Newton C. Birkhead,* Irwin J. Fox,* and Earl H. Wood. Mayo Fndn., and Mayo Clinic, Rochester, Minn.

The effect of varying the dye dose on the contour and time components of indicator dilution curves is of both academic and practical importance. To study this effect, arterial dilution curves were recorded continuously by a curvette oximeter at a femoral artery after successive, sudden, single injections of 3 different dosage levels of a single indicator into the pulmonary artery in 11 anesthetized dogs breathing 100% oxygen. Three different indicators were used (T-1824, indigo-carmine and tricarbocyanine dye II). Quantities of the indicator amounting to one half, one and 1.5 or 2 times the usual dose were injected in succession in random order. Immediately after recording of these 3 dilution curves, which required 20-30 min, a 4th curve was recorded, with use of one of the previous dose levels as a control to obtain data about spontaneous variability between successive dilution curves. Cardiac output values by Stewart-Hamilton methods averaged 2.9, 2.9, 2.7 and 2.8 l min for the small, middle, large and repeat control doses, respectively. The likelihood of statistical significance for the difference between the small and large, and middle and large values approached 95%. Peak concentrations of the curves expressed as mg/l/mg of dye injected/kg of body weight were not significantly different at the different dose levels. The appearance times, peak concentration times and systemic recirculation times of the curves also were not affected. These results give added support to the validity of indicator-dilution methods.

USE OF AET AS A PROTECTIVE AGENT AGAINST WHOLE-BODY X-RADIATION DEATH IN DOGS. L. T. Blouin*, B. G. Crouch* and R. R. Overman. Clin. Physiology Labs., Univ. of Tennessee College of Medicine, Memphis.

The sulfhydryl compound S, β -aminoethylisothiuronium · Br · HBr (AET) has been clearly demonstrated to protect mice and monkeys from otherwise lethal doses of whole-body x-radiation. The present study was conducted to determine the ability of AET to protect mongrel dogs from death as a result of whole-body x-radiation in lethal doses (500 r). The AET was administered by stomach tube immediately prior to the x-ray dosage. Preliminary toxicity studies indicate that as much as 300 mg/kg body weight can be given to anesthetized dogs, and 600 mg/kg body weight to unanesthetized dogs without serious toxic effects. Two groups of animals were used. The first of these was comprised of dogs anesthetized with 20 mg/kg body weight of sodium pentobarbital then treated with AET and subjected to x-radiation. The second group consisted of dogs trained to receive the AET dosage without undue excitation, and then to lie quietly in a box for the irradiation procedure. The blood picture of unprotected dogs subjected to whole-body x-radiation in lethal and sublethal doses has been previously studied. During the present investigations, the following variables were measured prior to and following the AET-irradiation procedure: total leucocytes, reticulocytes, platelets, differential white cell counts, hemoglobin, hematocrit and sedimentation rate. Other variables followed were blood pressure, heart rate, rectal temperature, body weight, unipolar electrocardiograms and gross autopsy observations.

EFFECTS OF POTASSIUM CHLORIDE UPON CARDIAC CLYCOGEN FRACTIONS IN DOGS. Don H. Blount and Arthur W. Merrick (intr. by Dallas K. Meyer). Dept. of Physiology and Pharmacology, Univ. of Missouri, Med. Ctr., Columbia.

Hyperpotassemia was induced in 10 anesthetized adult mongrel dogs of either sex by infusion of isotonic KCl in the right of femoral vein. Infusion rate was based upon the weight of the animal so that the duration of the infusion averaged 2 hr. At the appearance of bizarre complexes in the electrocardiogram the heart was quickly excised and each chamber analyzed for acid-soluble and acid-insoluble glycogen according to standard procedures. Blood samples were drawn frequently and the serum analyzed for potassium by flame photometry. Glycogen control values were obtained from 10 animals subjected only to anesthesia (sodium pentobarbital) for 2 hr. The mean acid-soluble glycogen values in mg % for the control animals were as follows: right auricle (RA), 588; left auricle (LA), 801; right ventricle (RV), 680; left ventricle (LV), 565. The mean acid-insoluble glycogen values were: RA, 84; LA, 144: RV, 118; LV, 75. Total glycogen was obtained by the addition of the 2 fractions. A statistical analysis of the 2 fractions and the total revealed there was no significant difference in any heart chamber following hyperpotassemia. This finding supports the view that hyperpotassemia in vivo does not result in the synthesis of cardiac glycogen. Minimal to moderate doses of potassium chloride in vitro are presently being investigated with dog cardiac tissue. (Supported in part by Grant H-2430(C) from the Natl. Heart Inst., USPHS.)

ACTIVITY OF ANGIOTONIN, PAPAVERINE AND OTHER DRUGS ON THE CORONARY ARTERIAL BED OF THE DOG. J. R. R. Bobb and Harold D. Green. Dept. of Physiology and Pharmacology, Bowman Gray School of Medicine, Winston-Salem, N.C.

The recently developed square wave electromagnetic flowmeter (Denison and Spencer, Rev. Sci. Instr. 27: 707, 1956) was used to measure the blood flow in a branch of the anterior descending coronary artery. The drugs were put directly into the coronary artery by placing them in the blood between the meter and the coronary cannula. Several were also injected into the femoral vein. Control determinations were done using epinephrine (1, 3, 10 μg), sodium nitrite (3 and 10 mg) and vasopressin (1 or 2 units). Test determinations of angiotonin (2 units), papaverine (100, 300 and 1000 μg), aminophyllin (1-3 mg) and other drugs were done. The responses to the control determinations were typical of the well established actions of these drugs. Angiotonin was found to be a potent constrictor of the coronary bed. Unit for unit, it was somewhat less active than vasopressin. Aminophyllin gave a response similar to epinephrine but with less effect on the strength of contraction. Papaverine was one of the most active of the dilating agents. Besides increasing coronary flow, it also caused some increase in the strength of contraction as shown by a decreased inflow or a backflow in the isometric contraction phase of systole. However, the latter effect was much less than that seen with epinephrine. (Supported by grants H2718 and H-487 of the Natl. Heart Institute, USPHS.)

QUANTITATIVE HISTOCHEMISTRY OF THE HUMAN NEPHRON: TECHNIQUES AND PRELIMINARY RESULTS. Sjoerd L. Bonting and Robert M. Kark (intr. by Ruven Greenberg). Dept. of Medicine, Presbyterian-St. Luke's Hosp., and Depts. of Biological Chemistry and Medicine, Univ. of Illinois College of Medicine, Chicago.

The purpose of this investigation is to determine quantitatively the activity of various enzymes in the different functional units of the human nephron, and correlate the findings with normal and pathological renal function. The ultramicro techniques developed by O. H. Lowry et al. for the brain have been adapted for use with kidney biopsy material. The biopsy is frozen rapidly in liquid nitrogen. Sections are then cut in a microtome cryostat at -20°C and freeze-dried. Single glomeruli, proximal tubules, distal tubules etc. are dissected out free-hand with microscalpels under a stereoscopic microscope (40 X magnification). Ultraviolet light of 360 mμ is used to distinguish between proximal and distal tubules: the former fluoresce dark blue and the latter bluish white. The specimens are weighed on a quartz fiber balance with a sensitivity of 0.3 mγ and a useful range of 15 to 150 mγ. They are then transferred to microtest

tubes, and incubated at 37°C with from 0.5 to 10 μl of a medium, containing the substrate, buffer, and any coerzymes and cofactors needed for the enzyme reaction. After incubation the amount of product formed is determined either spectrophotometrically in microcuvettes, or fluorometrically. (Supported by a U. S. Army research grant.)

GASTRIC POTENTIAL AND RESISTANCE FOLLOWING REESTABLISHMENT OF BLOOD FLOW. Allan Bornstein*, Warren H. Dennis* and Warren S. Rehm. Depts. of Physiology and Chemistry, University of Louisville, Ky.

Previous results have shown that interruption of the blood supply to the dog's stomach results in a fall in P.D. and an increase in resistance. Following reestablishment of the blood flow, the P.D. and resistance change rapidly during the first few minutes. With the previous technique, it was not possible to follow, accurately, these rapid changes. The purpose of the present work was to determine the P.D. and resistance during this period, using the chambered gastric segment preparation. The P.D. across the stomach was measured with a recording potentiometer. Resistance was measured by determining the effect of small currents on the P.D. Following reestablishment of blood flow, the P.D. started increasing within 1 sec and peaked at about 2/3 of its control level, within 20-40 sec. It then decreased to about half of the control level within a minute and then slowly increased to its control level. The resistance, during the interruption of blood flow, was about twice its control value. Following the reestablishment of the blood flow, there was little change in the resistance by the time the P.D. was over half way to its peak. From the time the P.D. was nearing its peak to the time when the P.D. had declined by a few mv, the resistance decreased to almost its control level. The resistance, after reaching its control level, remained there during the slow rise in the P.D. (Supported by Army Contract and by grant from NIH.)

EFFECTS OF NEGATIVE PRESSURE BREATHING ON RENAL EXCRETION OF FREE WATER AND TOTAL SOLUTE. John W. Boylan and Dorothy E. Antkowiak (intr. by H. Rahn). Dept. of Physiology, Univ. of Buffalo School of Medicine, and Cardio-Renal Lab., E. J. Meyer Memorial Hosp., Buffalo, N.Y.

Gauer, Henry, Sieker and Wendt described diuresis in response to continuous negative pressure breathing in the dog, an observation later extended to man (J. Clin. Invest. 33: 572, 1954) and confirmed in both species by Surtshin and others (Am. J. Physiol. 180:612, 1955). All of the above experiments were carried out under conditions of moderate hydration. We have extended these observations to include 1) moderate hydration, 100 cc H_2O every 1/2 hr., 2) hydropenia, at least 12 hr without water; 3) maximal, sustained water diuresis; and 4) moderate hydration plus infused Pitressin. The subjects were volunteer medical students in apparent health who were exposed to negative pressure breathing at -15 cm H_2O for 30-45 min. Results confirm the diuretic effect noted by others in condition 1. This is associated with an absolute increase in the excretion of free water and occurs without change in plasma osmotic pressure. GFR (inulin) and RPF (PAH) both rise in the first 15 min of negative pressure breathing, but return to control levels thereafter. These values are invariably depressed in the initial recovery period. In the hydropenic state (2) one of two results may obtain. There may be no change or an increase in urine flow which parallels an increased solute excretion without change in the free water clearance. This latter effect is seen occasionally and unpredictably in condition 1. Results obtained during maximal water diuresis (3) and hydration plus Pitressin infusion (4) have been more variable.

OCCURRENCE OF INTRAVENTRICULAR DIASTOLIC SUCTION WITH NORMAL ARTERIAL PRESSURES. Gerhard A. Brecher and Abbott T. Kissen*. Dept. of Physiology, College of Medicine, Ohio State Univ., Columbus.

It has been established recently that the mammalian and reptilian ventricle is capable of drawing fluid into its cavity during diastole (Bloom, Kraner and Ogden, Bloom and Ferris, Brecher). However, the existence of such diastolic

ventricular vis a fronte could be demonstrated only under experimental conditions in which the ventricle was nearly empty since it ejected against an almost pressureless arterial system. The question remained unresolved whether a ventricle with a more nearly normal residual volume draws blood into its cavity during diastole. In open-chest dogs the heart was submerged by filling the chest with donor blood. The left atrial wall was extirpated permitting the pulmonary veins to empty into the chest. Thereby, zero ventricular filling pressure was established. The entire circulation and arterial pressures were maintained at normal levels by pumping pulmonary venous blood from the chest cavity into the femoral artery. The normal aortic pressure level determined the resistance to ventricular ejection and thereby prevented the end-systolic residual ventricular volume from decreasing markedly. Under these conditions small systolic aortic pressure pulses were recorded indicating the existence of ventricular ejection. These ejections were enhanced in the normal and failing heart by the action of epinephrine. Since the ejected blood must have entered the ventricle with zero filling pressure, it was concluded that part of the filling of the ventricle working against normal aortic pressures is caused by a ventricular diastolic vis a fronte, and that this force is increased by positive inotrope drugs.

BILE INJECTION INTO PANCREATIC DUCT: EFFECT ON BLOOD SUGAR. A. B. Bridgwater*, and H. Necheles. Dept. of Gastrointestinal Research, Michael Reese Hosp., Chicago.

Upon injection of bile into the pancreatic duct of 5 non-fasted dogs, an overall increase in blood sugar of 40 - 138 mg % (average: 87) was observed. These increases became maximal within 10 - 20 min after operation and the blood sugar returned to the pre-operative level within 1 - 3 hr. The same procedure was carried out on 6 dogs fasted 2-3/4 - 4 days. Here, the increases varied from 3 to 128 mg % (average: 49.5) and became maximal within the same time as in the non-fasted animals. The data suggest an epinephrine effect but are not conclusive. To this end, the same experiment is being repeated on a series of dogs with their adrenal medullas removed. It is surprising that with so much edema, destruction of the pancreas and hemorrhage, no hyperglycemia was observed after 24 hr. (Supported by grant from USPHS.)

EFFECTS OF SELECTIVE LESIONS IN LOWER BRAIN STEM ON X-IRRADIATION EMESIS IN THE DOG. Kenneth R. Brizzee (intr. by Thomas F. Dougherty). Dept. of Anatomy, Univ. of Utah College of Medicine, Salt Lake City.

In control series 9 dogs were exposed to total body x-irradiation at a dose of 1200 r. Emesis occurred in 3 of these animals during the course of the radiation and the remaining 6 vomited between 15 and 98 min following radiation. The experimental series consisted of 11 dogs in which bilateral lesions were placed in area postrema (4) dorsal sensory vagal nucleus (4) or the junction zone between the lower vestibular nuclei and nucleus gracilis (3). Following a recovery period of at least 2 wk the operated animals were exposed to total body x-irradiation at 1200 r. Ablation of area postrema resulted in protection of 3 of the 4 animals in this group against x-irradiation emesis. The unprotected animal vomited during the course of radiation and at 32 min after. Lesions in the dorsal sensory vagal nucleus protected only 1 of the 4 animals operated. One of the three unprotected animals in this series vomited during radiation while the other 2 responded at 60 and 93 min following radiation respectively. Lesions placed in the lower vestibular-gracilis zone failed to protect any of the 3 animals of this series, all of which vomited during the course of radiation.

DEMONSTRATION OF A DUAL CONTRACTILE RESPONSE OF THE ARTERY STRIP TO VARIOUS STIMULATING AGENTS. Donald C. Brodie*, David F. Bohr and Jeanette Smit*. School of Pharmacy and Dept. of Pharmacology, Univ. of California, San Francisco, and Dept. of Physiology, Univ. of Michigan, Ann Arbor.

Effects of drug concentration, temperature and adrenergic blockade on the contractile response of rabbit aorta were studied. Strips of aorta were mounted in chambers of Kreb's solution containing calcium EDTA (10^{-5}). Isotonic contractions were recorded on smoked paper. Concentration: dose response curves for each agent revealed a critical concentration at which the contractile response assumed a biphasic character. An initial fast shortening (F component) was followed by a more prolonged period of much slower contraction (S component). The usual shortening process seen with higher concentrations of the agent consisted of a fusion of the 2 components into a single continuous contraction. The biphasic character of the response to epinephrine and norepinephrine were essentially alike. Phenylephrine, however, at concentrations producing approximately 10% shortening of the strips elicited only the S component. Temperature: reduction in temperature affected the 2 components differently so that the F/S ratio was increased. Blockade: a differential blockade of the 2 components was evident when the strip was treated with dibenamine. The most plausible explanation for this biphasic response with its 2 distinguishable components is that the several constrictor agents studied activate 2 processes which progress at different rates but which both result in shortening of the smooth muscle of the strip. (Supported by Research Grant H-3146, NIH, USPHS.)

IMPEDANCE VARIATION WITHIN THE LATERAL HYPOTHALAMUS OF THE CAT. George W. Brown. Gen. Med. Research Lab., VA Hosp., Iowa City, Iowa.

Experiments were designed to test the hypothesis that electrical impedance between electrodes chronically implanted in brain tissue is a dynamic quantity. A series of cats was prepared with standardized electrodes implanted in the lateral hypothalamus. Impedance measurements were made at hourly intervals for a period of 30 days. Although each cat was subjected to as nearly identical operative conditions as possible it was found that each lateral hypothalamic nucleus exhibited an impedance level typical of that nucleus. During the postoperative period all impedance levels for all nuclei studied exhibited an elevation followed by a decrement. However, the percentage increase and decrement and the time required to reach a peak value was not the same for each nucleus. Thus it appears that the impedance level as well as the daily variation in impedance is an individual variable which must be assayed for each nucleus and electrode configuration being investigated. This individual variation is significant in studies involving cerebral stimulation and associated behavioral effects.

MODERATOR NERVE REFLEXES IN HUMAN HYPERTENSION. Ivan L. Bunnell, John T. Sharp, Donald M. Frey and David G. Greene (intr. by Fred R. Griffith). Dept. of Medicine, Buffalo Gen. Hosp., Univ. of Buffalo, N.Y.

The sensitivity of the moderator nerve reflexes in their regulation of heart rate was investigated in both normotensive and hypertensive human subjects. Changes in heart rate were reflexly produced by varying systemic blood pressure in several ways: administration of vasoconstrictor and vasodilator drugs, and the use of the Valsalva and Mueller maneuvers. Thirty-seven normontensive subjects performed Valsalva or Mueller maneuvers or both. The overall ratio of systolic pressure cahnge to pulse rate change ($\Delta P/\Delta R$) was determined to be 1.8. The comparable value in 22 hypertensive patients was 5.0, indicating that in hypertension the moderator nerve reflexes are less than normally effective in heart rate regulation. Similarly, the heart rate changes reflexly produced during norepinephrine infusion or amyl nitrite inhalation were much greater in 12 normotensive subjects than in 10 hypertensive patients; $\Delta P/\Delta R$ averaged 1.0 in normotensives as compared with a value of 4.1 in hypertensives. During this study a way of analyzing the hemodynamic response to the Valsalva and Mueller maneuvers was utilized which involved graphic representation of beat-to-beat changes in blood pressure and heart rate. This method of analysis facilitates understanding of mechanisms involved in the complex responses. In particular, it is possible by this means to infer the primacy of either the carotid sinus or aortic pressoreceptor systems in determining the circulatory responses to the Valsalva and Mueller maneuvers.

COMPARATIVE STUDY OF GROWTH-PROMOTING ACTIVITY OF VITAMIN B_{12} AND A CRYSTALLINE GRASSHOPPER PIGMENT. L. E. Burgess* and D. T. Rolfe. Physiology Dept., Meharry Med. College, Nashville, Tenn.

The isolation of a reddish-brown crystalline substance from the developing egg of the grasshopper has been reported (Arch. Biochem. 20:347, 1949). This crystalline substance exhibits infrared absorption spectra similar in character, but not identical, with the infrared absorption spectra of crystalline vitamine B_{12}. Our earlier studies demonstrated that this crystalline grasshopper pigment can replace crystalline vitamin B_{12} in the nutrition of certain lactic acid bacteria. The present investigation was designed to test the ability of the crystalline grasshopper pigment to replace vitamin B_{12} in depleted rats fed a casein-dextrin diet with iodinated casein. The basal diet was essentially the same as that used by Frost et al. (J. Nutrition, 49:107, 1952). The basal diet for the vitamin B_{12} depleted rats was supplemented, for 3 wk, with graded levels of either crystalline vitamin B_{12} or crystalline grasshopper pigment. Control animals received only the unsupplemented basal diet. The rats were fed ad libitum and weighed twice weekly. The results of the growth assay show a remarkably close similarity between the growth increments elicited by vitamin B_{12} and by samples of crystalline grasshopper pigments. The technique of preparation eliminates the possibility that the grasshopper pigment contained any traces of vitamin B_{12}. During preparation, the pigmented substance is recrystallized from 95% ethyl alcohol and the crystals are washed several times with cold distilled water. (Supported by grant from Natl. Inst. of Arthritis and Metabolic Diseases, USPHS.)

MICROSCOPIC DIMENSIONS OF THE DOG'S GASTRIC MUCOSA. Cipriano Canosa* and Warren S. Rehm. Depts. of Physiology and Chemistry, Univ. of Louisville, Ky.

In our studies on gastric HCl formation, there has been a recurring need for accurate data on the microscopic dimensions of the stomach. Because of the obvious objections to values obtained with conventional techniques, we used a method in which a flap of stomach, with an intact blood supply, was rapidly frozen with liquid nitrogen. Serial sections were cut parallel to the surface, observed and photographed in a room maintained at -18°C. The outlines of the pits were clearly discernible, while those of the tubules (except in the neck region) were not. For the pit region, average values as percentage of total area were: 46% for the area between the pits, 9% for the pit lumen area and 45% for the pit cell area. There were 1.1×10^4 pits/cm^2. The average distance between the pits was 98 microns. There was no significant difference between secreting and resting mucosa. The sections in some experiments, after they were photographed, were fixed and stained by the method of Papanicolaou. The dimensions of the pit region were essentially the same as before fixing and staining. Observation of the tubular region of the stained sections revealed that there was very little space between the tubules in the lower two thirds of the tubular region, and that the average radius of the tubular lumen was about 5 microns. (Supported by Army Contract and by grant form NIH, USPHS.)

TUBULAR SECRETION AND REABSORPTION OF ELECTROLYTES DURING PHOSPHATE LOADINGS. Gaspar Carrasquer*, John T. Kaim*, Robert L. Shapiro* and William A. Brodsky. Depts. of Physiology and Chemistry, Univ. of Louisville, Ky.

Loading dogs with buffered and unbuffered KH_2PO_4 induced reproducible patterns of excretion of K^+, Na, PO_4 and titratable acid. During acidosis, parallel patterns of excretion of the ions were noted. Under non-acidotic conditions, K, Na and PO_4 excretion changed in the same direction, while titratable acid remained constant. Estimated reabsorption and secretion of K and PO_4 were similar in most experiments. In 3 cases (with pre-feeding of KH_2PO_4) a progressive decrease in K and PO_4 reabsorption from positive to negative values occurred with increasing plasma levels of these ions. Our current hypothesis requires that $H_2PO_4^-$ and K^+ may be secreted into the lumen at the acidification site. This would not exclude phosphate reabsorption, along with cation, at a proximal tubular

site. In fact, it is mandatory that reabsorption of phosphate and potassium occurs, even when their clearances are greater than that of creatinine. Excretion of Na^+ (with a constant filtered load) increased with that of other ions. Assuming no sodium secretion, it is difficult to explain these data on the basis of forced exchanges between Na^+ and H^+, or between K^+ and H^+. Elements of the present scheme are: 1) proximal reabsorption of phosphate, like most anions, is related directly to that of Na^+; 2) no Na^+ ions are secreted; 3) secretion of $H_2PO_4^-$ and of K^+ occurs at the acidification site of the tubule. Calculations based on aforementioned assumptions indicate that secretion could account for 80-90% of urinary K^+ and $H_2PO_4^-$.

PERSISTANCE OF PULMONARY STRETCH RECEPTOR IMPULSES AFTER DEFLATION. John L. Chapin (intr. by Clarence A. Maaske). Dept. of Physiology, Univ. of Colorado, Denver.

Anesthetized dogs and rats were hyperventilated artifically and the duration of the ensuing period of apnea was measured. Durations of apnea exceeding 1 min could not be shortened by vagotomy. Durations shorter than 1 min could usually be shortened by vagotomy sometimes to 1/2 of the durations with vagi intact. Vagotomy at the end of the hyperventilation period and at the beginning of the apnea period resembled vagotomy before hyperventilation. This suggests that vagal firing throughout the period of apnea is necessary to provide sufficient inhibition for a long apnea.

HUMAN CEREBRAL HEMISPHERE FUNCTION. L. F. Chapman*, L. Berlin*, T. C. Guthrie*, W. N. Thetford*, and H. G. Wolff. Cornell Univ. Med. College, New York City.

Fifty-five subjects with loss of known amounts of cerebral hemisphere tissue were studied in their natural setting and in the laboratory to define more carefully impairment in the functions of the human cerebral hemispheres as evidenced in changes in mentation, attitudes, feeling and behavior. Those selected did not have significant defects in speech or motility function; their defects were not known to extend beyond the cortex and underlying white matter of the frontal, temporal or occipital lobes. They were studied by means of 1) extensive interviews in regard to life patterns before and up to 7 years after tissue loss, 2) intensive survey of the subjects' behavior including data collected from members of their families, neighbors and associates, 3) a large group of quantitiative behavioral assay procedures selected as measurements in the major dimensions of human behavioral capacity. Detectable and predictable reductions in capacity, both in the laboratory and in the broader life situation, were observed in these subjects even when the mass of tissue loss was small (20 gm). The range of capacities impaired was broad, i.e. defects were observed in 1) data about the expressions of needs, appetites, drives, motives etc.; 2) data about the integrative mechanisms of such goals; 3) data about resistance to disorganization during periods of stress. The loss of tissue from the cerebral hemispheres resulted in a generalized impairment of these functions, the degree being related closely to the mass of tissue loss regardless of site.

LESION FORMATION IN ARTERIES OF RATS FED A LATHYRUS DIET. Leo P. Clements (intr. by C. M. Wilhelmj). Creighton Univ. School of Medicine, Omaha, Nebr.

Lathyrism was induced in 14 rats as shown by x-ray of the spine, and paralysis of the hind quarters. The 7-10 or more concentric elastic membranes in the media of normal rat aortas are lined closely with a sheath of PA-Schiff-positive substance. The membranes stain with orcein and with the methyl green counter-stain after the PAS reaction. The inter-spaces, wider than the elastic membrane and sheaths, contain scattered connective tissue cells between large and small elastic fiber branches which cross the inter-space from one elastic membrane to the other. PAS-positive substance lines also the elastic fiber branches in the inter-spaces. In Lathyrus-fed rats there occur in sequence in local sites; 1) thickening of the aortic media, as in edema; 2) an increase in the

amount of PAS-positive substance in the inter-spaces; 3) a certain fragmentation and discontinuity of the elastic membranes and their sheaths; 4) formed rows of PAS-positive cartilage cells and capsules in the inter-spaces with further thickening of the media, and intima, and their nodular protrusion into the lumen; 5) the center of the nodule becomes fibrillar, or amorphus, around a few large cartilage lacunae, and the elastic membranes lose their identity as they run into this area; 6) an obvious fragility of the whole nodular area, giving rise in the intima and media to breaks and splits which communicate with the aortic lumen. The PAS-positive substance could not be identified conclusively. (Aided by a Nebraska Heart Association Grant.)

BIOCHEMICAL AND ELECTROENCEPHALOGRAPHIC CHANGES IN BRAIN OF RABBITS INJECTED WITH 5-HYDROXYTRYPTOPHAN. E. Costa, F. Rinaldi (intr. by Williamina A. Himwich). Thudichum Psychiatric Research Lab., Galesburg State Research Hosp., Galesburg, Ill.

Following intravenous injections of 5-hydroxytryptophan (75 mg/kg) in agreement with previous reports (Udenfriend S. et al., J. Biol. Chem. 224: 810, 1957) changes in behavior and increases in brain serotonin concentrations were observed in the different brain structures analyzed (cerebellum, neocortex, hippocampus, midbrain and medulla-pons). If the increase in brain serotonin concentrations were estimated in terms of multiples of their respective control values the smallest increase occurred in the cerebellum; the highest rise was seen in the hippocampus. Electrical activity recorded from different brain structures disclosed changes following injection of 5-hydroxytryptophan. Hippocampal theta alert rhythm, spindles and other normal sleep features disappeared. A generalized fall in the voltage with random abnormally slow waves was also observed. Minor variations of blood pressure and electrocardiogram were noted during the 2 hr following the administration of 5-hydroxytryptophan. Injections of comparable amounts of 5-methyltryptophan neither caused changes in behavior nor increased the serotonin concentrations of the brain structures examined. The EEG pattern does not change after treatment with 5-methyltryptophan. The biochemical data illustrating the hippocampus as an important district of indole metabolism should be considered with caution. Besides differences in the rate of decarboxylation of 5-hydroxytryptophan the intensity of serotonin catabolism will be discussed as a determining factor of the observed variations in serotonin content of various brain parts after injection of the serotonin precursor.

EFFECT OF NEGATIVE INTRA-ALVEOLAR PRESSURE DURING BREATH-HOLDING ON PULMONARY DIFFUSING CAPACITY AS DETERMINED BY THE SINGLE BREATH METHOD. J. E. Cotes*, D. P. Snidal* and R. H. Shepard. Depts. of Environmental Medicine and Medicine, Johns Hopkins Univ., Baltimore, Md.

The diffusing capacity of the lungs (D_L) was measured by the single breath method (Forster, R. E., et al., J. Clin. Invest. 33: 1135, 1954) at different intra-alveolar pressures in 2 normal subjects at rest and 10 sec after strenuous treadmill exercise. Rate of inspiration was controlled. Breath holding (open glottis) occupied 10 sec. Intra-alveolar pressure was made negative during breathholding by inspiratory effort against a manometer. Capillary volume (V_C) and membrane diffusing capacity (D_M) were calculated from D_L at 2 levels of $F_{I_{O_2}}$ using the relationship $\frac{1}{D_L} = \frac{1}{D_M} + \frac{1}{\theta V_C}$ (θ = reaction rate between CO and hemoglobin), (Ogilvie, C. M., et al., J. Clin. Invest. 36: 1, 1957). In one subject, D_L did not change with 30 mm. Hg negative pressure. In the other subject it rose progressively from 30.5 to 40.9 units (134%) at rest when the intra-alveolar pressure varied between atmospheric and -24 mm. Hg. After exercise the same variation in pressure was associated with an increase of from 44.5 to 50.3 units (113%). The magnitude of change varied with lung volume. Two sec of negative pressure at the beginning, middle and end of breathholding also increased D_L (mean increases at rest 15%, 9%, and 7% respectively). The increase in D_L appeared to result largely from an increase in V_C, although some increase in

D_M cannot be excluded. It is concluded that a negative intra-alveolar pressure during breathholding may be a source of error in the estimation of D_L by the single breath method.

PRECENTRAL AND SUPPLEMENTARY MOTOR AREAS OF ATELES. W. S. Coxe*, J. F. Hirsch*, R. M. Benjamin*, W. I. Welker*, R. F. Thompson* and C. N. Woolsey. Lab. of Neurophysiology, Dept. of Physiology, Med. School, Univ. of Wisconsin, Madison.

The discrepancy between the extent of the precentral motor face area, as defined by Fulton and Dusser de Barenne, and the face subdivision of the tactile area, as mapped by Chang et al., has been resolved by showing that the precentral area occupies the rostral part of the face region, while the tactile area lies in the caudal part. Motor responses can be obtained from both. The motor pattern of the tactile area parallels the tactile pattern and is essentially a mirror image of the precentral motor pattern. The precentral motor area occupies the entire width of the broad precentral gyrus. The epiaxial musculature and proximal parts of the limbs are represented rostrally, as in Macaque, while distal parts are represented nearer the central sulcus. Representation for the proximal musculature appears greater than in Macaque, consonant with the greater use of this musculature in brachiation. The medial-lateral extents of the major subdivisions are as described by Fulton and Dusser de Barenne. The supplementary motor area occupies the mesial aspect of the hemisphere, as in Macaque, but is more accessible, since the precentral motor area does not reach the cingulate sulcus. There is good definition of face, arm and leg subdivisions, but the pattern defined in less differentiated than in Macaque. Responses also were obtained on stimulation of the anterior cingulate gyrus. (Supported by Grant B-732 NINDB.)

IMPORTANCE OF HEMATOCRIT RATIO IN HEMORRHAGIC SHOCK. Jack W. Crowell and Sara Bounds (intr. by Arthur C. Guyton). Dept. of Physiology and Biophysics, Univ. Med. Ctr., Jackson, Miss.

By the use of 1) acetyl phenylhydrazine, 2) hemorrhage, 3) transfusion and 4) natural variation, 67 dogs with hematocrit ratios varying from 12 to 56 were obtained. These dogs were subjected to hemorrhagic shock by lowering their arterial blood pressure to 30 mm Hg, and the time lapse between the initial production of hypotension and the beginning deterioration of the animal determined. This time lapse is a measure of the resistance of the animal to the development of irreversible shock. A graph of initial hematocrit versus the time required for the development of irreversible shock shows that an increase in the hematocrit ratio from 12 to 35 increases the resistance of the animals by a factor of approximately 5; however, increasing the hematocrit ratio above 35 decreases the resistance of the animal to the development of irreversible shock. A possible explanation for these results is as follows: the maximal amount of oxygen a tissue can receive is a function of blood flow times the oxygen carrying capacity of blood. The control of tissue pH depends upon the buffer capacity of blood times the blood flow. Increasing the hematocrit ratio increases both oxygen carrying capacity and buffer capacity; however, an increase in the hematocrit ratio increases the blood viscosity and decreases blood flow. Thus, an optimal value of the hematocrit ratio may exist for tissue oxygenation and for tissue buffering. (Supported by grant from the Natl. Heart Inst. USPHS.)

EFFECTS OF CHLORPROMAZINE ON SMALL INTESTINAL TRANSIT. Ivan E. Danhof (intr. by John C. Vanatta). Dept. of Physiology, Univ. of Texas Southwestern Med. School, Dallas, Texas.

Chlorpromazine administration in dogs causes a primary increase in duodenal motility lasting from 30 to 60 min followed secondarily by a decreased motility lasting at least 3 hr (Staff. Meet. Mayo Clinic 30: 601, 1955). Diminished tone and motility were observed in the isolated rat and rabbit ileum (Compt. rend. Soc. de Biol. 168: 565, 1954). The in vivo effects of chlorpromazine on intestinal transit were studied in the rat. Two groups of 24 albino male rats, each weighing

250 - 300 gm, were fasted 18 hr and given a charcoal-acacia mixture by stomach tube in a dosage of 2% of body weight. This was followed immediately by the intraperitoneal administration of 0.5 cc of saline to the control group and equivolume of chlorpromazine (25 mg/kg) to the experimental group. The intestinal transit was measured at 5, 15 and 30 min following the injections expressing the distance the charcoal-acacia mixture was propelled as a percentage of the total small intestinal length. The control group transit values were found to be 65.7, 74.1, and 83.7% at 5, 15 and 30 min, respectively, while the experimental group transit values were observed to be 33.4, 36.3 and 49.6% when measured similarly. The 2 groups were significantly different at the 0.01 confidence level. The data indicate that chlorpromazine markedly depresses the intestinal transit and fail to show a primary in vivo enhancement of intestinal transit in the rat.

EFFECTS OF A BODY CAST ON ALDOSTERONE AND SODIUM EXCRETION IN DOGS WITH EXPERIMENTAL ASCITES. James O. Davis and Wilmot C. Ball, Jr.* Natl. Heart Inst., Bethesda, Md.

The increased rate of aldosterone secretion in dogs with ascites secondary to thoracic inferior vena cava constriction has been related (J. Clin. Invest. 26: 689, 1957) to factors associated with the extravasation of fluid and electrolytes from the blood stream. The present study was undertaken in an attempt to inhibit or prevent the loss of fluid into the peritoneal cavity by application of a body cast and to determine the effects on aldosterone and sodium output. Observations were made in 8 mongrel dogs. After a control period, abdominal paracentesis was performed and a body cast was applied. After 6-9 days the cast was removed and observations were made during a recovery period. During the period of the cast, a progressive increase in intra-abdominal pressure (indicated by a rise in inferior vena caval pressure) occurred, urinary aldosterone excretion dropped and sodium excretion increased. In 3 animals, sodium balance became negative. The increased sodium excretion was not attributable to elevated GFR because GFR was unchanged or reduced. Instead, the data support the interpretation that aldosterone secretion was decreased sufficiently to effect an increase in sodium excretion and, in 3 instances, net sodium loss.

EXPERIMENTAL FROSTBITE PRODUCED BY AIR COOLING. T. R. A. Davis, D. R. Johnston and C. A. Silver (intr. by G. W. Molnar). US Army Med. Research Lab., Fort Knox, Ky.

In all but a few instances, experimental frostbite has been produced by immersion in cooled liquids such as isopropyl alcohol. Isopropyl alcohol has a heat transfer coefficient 38 times greater than that of air. It can be shown theoretically that these differences in rates of cooling are such that slower air cooling results in axial temperatures which closely follow surface temperatures in a 2 cm cylinder having the average thermal properties of tissue. On the other hand, with rapid cooling, surface temperatures can reach low temperatures very rapidly with very little or no change in axial temperatures. Thus it is probable that the characteristics of frostbite produced by rapid cooling may be quite different from those produced by air cooling. In air cooling a great variability existed both in eventual tissue loss and in time it took different animals (rabbits) to freeze. This variability was shown not to be associated with the conditions of the experiment and it could not be explained by the known laws of thermodynamics. Thus it was presumed to be due to physiological responses brought into play to prevent tissue freezing. It was shown that after freezing had occurred, a high degree of association existed between the temperatures to which tissues were frozen and tissue loss (-0.92) but that no association at a significant level existed between tissue loss and duration in the frozen state. It was also shown that the degree of existence of the hunting phenomenon did not correlate with time taken to produce freezing or with eventual tissue loss.

IMPEDANCE OF THE GASTRIC MUCOSA. Warren H. Dennis* and Warren S. Rehm. Depts. of Physiology and Chemistry, Univ. of Louisville, Ky.

Previous studies on the variation, with frequency, of impedance of the amytalized dog's stomach have been extended. A square wave technique has been used to determine the high frequency impedance and the low frequency impedance in a short-time interval. The technique allows one to estimate the parallel resistance of the Cole-Lullies equivalent circuit as the difference between the low and high frequency impedances. In the non-acid secreting stomach, the parallel resistance is about 60 ohms cm^2. If the blood supply is interrupted, there is a marked rise in the low frequency impedance with most of the rise occurring in the parallel resistance, which rises to 400 ohms cm^2. Twenty-four hr after interruption of the blood supply, the low frequency impedance has fallen to about the level of the acid secreting stomach, and there is essentially no reactance. This impedance level is very close to the series resistance of the non-acid secreting stomach which is about 300 ohms cm^2.

FUNCTIONAL EVISCERATION AND METABOLIC RESPONSE OF ANESTHETIZED WARM AND COLD ACCLIMATED RATS EXPOSED TO COLD. Florent Depocas (intr. by J. Sanfort Hart). Natl. Research Labs., Div. of Applied Biology, Ottawa, Canada.

The effect of functional eviscera tion (ligation of colon, coeliac and superior mesenteric arteries, and portal vein) on the O_2 consumption of barbital anesthetized warm and cold acclimated rats (J. Appl. Physiol. 9: 399, 1956) at 30°C and on exposure to 6°C has been examined. At 30°C, cold acclimated rats had a significantly higher oxygen consumption than warm acclimated rats but after eviscera tion the lower level reached was the same in both groups. When sham operated animals at 30°C were transferred to an environment at 6°C, the O_2 consumption increases were 95 and 180% respectively in the 2 experimental groups. When the animals were functionally eviscerated just before transfer to the cold environment the increases were 62% for the warm acclimated and 285% for the cold acclimated rats, of the O_2 consumption of similar eviscerated rats at 30°C. These results indicate that either through shivering alone or non-visceral chemical thermogenesis plus shivering, functionally eviscerated anesthetized cold acclimated rats increased their O_2 consumption on exposure to cold as much as similar non-eviscerated rats at the same apparent level of shivering. Warm acclimated rats which shiver more under the same conditions show a much poorer response.

RESPONSES TO EXERCISE AS RELATED TO AGE. D. B. Dill, S. M. Horvath and F. N. Craig. Directorate of Med. Research, Chem. Warfare Labs., Army Chem. Ctr., Md., and Dept. of Physiology, State Univ. of Iowa, Iowa City.

Robinson (Arbeitsphysiol. 10:261, 1938) has studied metabolic and circulatory responses to exercise in boys and men from ages 6-90. During the past year one of Robinson's subjects, D.B.D., now age 66, has participated as a subject in exercise experiments similar to those in which he was a subject 25-32 years ago. During this period, his basal heart rate, oxygen consumption and blood pressure have remained unchanged. His highest attainable oxygen intake in exercise has declined from 3.3 to 2.8 l/min and his maximum heart rate in exercise from 172 to about 160.

LYMPH FLOW STUDIES IN UNANESTHETIZED DOGS HAVING CHRONIC THORACIC DUCT-JUGULAR VEIN CANNULATIONS. D. B. Doemling* and F. R. Steggerda. Dept. of Physiology, Univ. of Illinois, Urbana.

The thoracic duct was cannulated with polyethylene tubing (PE-100, Clay-Adams, I.D. .86 mm X O.D. 1.52 mm) near its connection to the venous system. The tip of the tube was slightly flared and the ligature was placed near the tip. This procedure prevents the lymph from stagnating around the indwelling portion of the cannula. The tube was exteriorized by way of a stab wound and connected by a short piece of larger tubing (PE-200) to another cannula (PE-100) which had been inserted into the right jugular vein (cf. Brown and Hardenbergh, 1950). No anticoagulant was necessary. Tubular orthopedic stockinet was used to protect the exteriorized loop of tubing. During collection periods, with the

dog lying on its left side, the loop of tubing was separated and the lymph drained into a graduated cylinder. The jugular cannula was used for infusing solutions in some instances. Some dogs had previously been prepared with an intestinal fistula (Thomas) and/or a cannula in the hepatic portal vein. The hepatic portal cannula (PE-200) was inserted by way of an intestinal vein and exteriorized at the back of the neck. When not in use this cannula was filled with saline and the end sealed. This preparation affords a means of studying thoracic duct lymph flow in trained dogs under physiological conditions. Results of experiments comparing the effects of the administration of saline by various routes as well as the effects of heparin and Adrenalin Chloride on lymph flow will be presented.

PHYSIOLOGICAL BASIS FOR METABOLIC GRADIENT OF THE SMALL INTESTINE. H. L. Dorman* and F. R. Steggerda. Dept. of Physiology, Univ. of Illinois, Urbana.

As indicated in a previous report, the isolated smooth muscle layer of the intestine does not present a detectable aboral metabolic regression as measured by the Warburg technique. However, the metabolic gradient of intact intestinal segments is clearly demonstrated by the same technique, and it is found to have a regression coefficient of 1.37 μ1/gm/hr/cm of intestinal length. Removal of Meissner's ganglionic plexus by mechanical separation or poisoning with hexamethonium chloride ($5x10^{-4}$M) completely abolishes the gradient. Following the removal of Auerbach's plexus the gradient of the otherwise intact preparation is reduced but not abolished. It is concluded that the metabolic gradient of intact intestinal segments observed in these experiments is primarily a result of the metabolic activity of the smooth muscle cells when they are in contact with the intrinsic ganglia of the intestine.

ADAPTATION OF THE RECORDING DYE DENSITOMETER (BALTIMORE) FOR WORK IN THE NEAR INFRARED REGION. Philip Dow and Irving Green*. Dept. of Physiology, Med. College of Georgia, Augusta.

Through the generosity of Dr. I. J. Fox, we have been able to work with a sample of the infrared-absorbing intravascular dye reported by him at the last spring meeting. The densitometer introduced by Milnor et al. is given infrared sensitivity by replacing the 931-A multiplier phototube with a DuMont #K-1292. Electrically, the new tube fits into the circuit very neatly. Physically, an entire new housing has been required which will probably limit some of the work in close quarters that was formerly possible. The biggest problem has been the optical one, the isolation of a spectral band narrow enough to give a satisfactory linearity of response. The best combination in preliminary studies includes a Wratten #87 and Pittsburgh Solex glass. The sensitivity of the tube is excellent, and the possibility is being explored that it may even serve better than the 931-A for T-1824 as well as for the Mayo-Eastman "Dye 2." (Supported by Grant H-240 from USPHS, and Life Insurance Med. Research Fund.)

MANNER OF ELIMINATION OF METABOLIZED $C^{14}O_2$ FROM THE BODY. Douglas R. Drury and Mary Carol Almen*, Dept. of Physiology, School of Medicine, Univ. of Southern California, Los Angeles.

The respiratory elimination of $C^{14}O_2$ was studied under 3 different conditions: 1) during administration of the tagged compound by constant intravenous infusion, 2) during constant infusion in the left ventricle, 3) after equilibrium had been established in the body after a single injection of the labeled compound. We find that mixing of $C^{14}O_2$ in the body is a rather sluggish process requiring 10-20 min to approach a steady state condition. CO_2 produced in the body is eliminated much faster than the $C^{14}O_2$ in condition 3. This indicates that CO_2 produced in tissues with a high blood flow is largely eliminated before mixing with the CO_2 pool of the body. $C^{14}O_2$ produced in such tissues during metabolism studies using C^{14} labeled fuels would be eliminated at a much faster rate than would be expected on the assumption that rapid mixing of CO_2 takes place in the body. (Supported in part by grant A-52-C5 from Natl. Inst. of Arthritis and Metabolic Diseases, USPHS.)

EFFECT OF TOLBUTAMIDE ON GLUCOSE UTILIZATION BY LEUCOCYTES OF PATIENTS WITH DIABETES MELLITUS. Mary E. Dumm and Roy C. Gumpel*. Dept. of Medicine, College of Medicine, New York University-Bellevue-Medical Center, New York City.

We have previously reported that the leucocytes of patients with diabetes mellitus who require more than 30 units of insulin per day have lower rates of glucose uptake (0.22 ± .04 μmol/hr/10^7 cells) than do leucocytes from either fasting (0.35 ± .03) or nonfasting (0.45 ± .04) normal subjects. Insulin added in vitro significantly increased glucose uptake by the leucocytes of normal subjects (+.07 μmol) and of insulin-dependent diabetics (+.09 μmol). The rate of glucose uptake by the leucocytes of mild diabetics requiring little or no insulin did not differ significantly from that of normal subjects and was relatively insensitive to insulin added in vitro. A group of mild diabetics have been given 1 gm of tolbutamide intravenously and the rate of glucose uptake and the sensitivity of the leucocytes to added insulin compared before and 2 hr after the tolbutamide was administered. Before the tolbutamide was injected glucose uptake averaged .41 μmol/hr without added insulin and .43 μmol/hr with added insulin. Two hr after tolbutamide was administered intravenously glucose uptake averaged .44 μmol/hr without added insulin. When insulin was added in vitro glucose utilization rose to .52 μmol/hour. The data suggest that in certain patients tolbutamide may cause an increased sensitivity of the cells to insulin added in vitro.

LINKAGE OF ACTIVE CATION TRANSPORT TO ATP UTILIZATION. E. T. Dunham (intr. by C. A. M. Hogben). Natl. Heart Inst., Bethesda, Md.

Active K influx and Na efflux persist long after endogenous glucose has disappeared from human erythrocytes suspended in glucose free media. A gradual decline in these fluxes is accompanied by an initially steeper decline in ATP. After depletion of hexose-phosphates, the only significant known energy reserves are 2,3-diphosphoglycerate (2,3 DPG) and ribotides. Pyruvate is no longer reduced; 2,3 DPG disappearance and pyruvate appearance have been the principal measurements used in the estimation of "energy-rich" phosphate (~P) production. ~P utilization has been determined by summing ~P production and net ~P loss. A quantitative relationship between ~P utilization and active transport has been observed. If iodoacetate is added to hexose depleted cells, subsequent addition of glucose might competitively inhibit any reaction drawing upon ~P. Results have shown severe depression of K influx by iodoacetate (10^{-3}M + glucose (200 mg%), but little effect by iodoacetate alone. Profound depletion of ATP resulted from hexose phosphorylation. Production of pyruvate from 2,3 DPG was unaltered by iodoacetate or iodoacetate + glucose. It is concluded that active cation transport is linked to ~P utilization, and the reactions involved in ~P production relate to transport only to the extent that they supply or remove ~P. A rise in ADP during the initial phase of declining transport (after hexose depletion) favors ATP as the principal ribotide from which ~P energy is removed for transport work. Transport utilization of ATP via an ATPase associated with the erythrocyte membrane is suggested by similar relative responses of active transport and of enzyme activity to pH (pH 6-9).

BLOOD FLOW IN THE DOG FOOT DURING RAISED INTRACRANIAL PRESSURE. H. E. Ederstrom, Bennie Faul* and Robert Welsh*. Dept. of Physiology and Pharmacology, Univ. of North Dakota Med. School, Grand Forks.

The work of Cannon and others has indicated that sympathectomized structures develop increased sensitivity to circulating epinephrine. However, infusion of synthetic epinephrine or nor-epinephrine into the aorta of a chronically sympathectomized dog was reported to have similar constrictor effects on normal and operated legs. Since raising the intracranial pressure (ICP) supposedly releases epinephrine from its sites of origin in the body, this procedure was applied to a group of dogs with sympathectomized and denervated hind legs. Venous outflow was used as a measure of blood flow. Raising the ICP to 200 mm Hg for two minutes caused about the same percent decrease in blood flow in normal and chronically sympathectomized hind legs. Similar results occurred when

acutely sympathectomized animals were used. Acute motor denervation of one hind leg was produced by sectioning of the femoral and sciatic nerves. When subjected to increased ICP, blood flow decreased about the same in both legs. Typical rises in blood pressure and bradycardia were found on raising the ICP. The results suggest that decreased blood flows in the sympathectomized and denervated legs were due to circulation of vasoconstrictor substances, probably epinephrine or nor-epinephrine, released during the high ICP.

THE EFFECTS OF GAMMA-AMINOBUTYRIC ACID (GABA) AND THIOSEMICARBAZIDE ON NEOCORTICAL EVOKED POTENTIALS. E. Eidelberg, W. Hyman, E. K. Killam, J. D. French (intr. by H. W. Magoun). Univ. of California at Los Angeles, School of Medicine, and VA Hosp., Long Beach.

The local cortical, transcallosal, direct projection and recruiting responses were studied in rabbits, cats and monkeys. Monopolar recording techniques were used throughout. It was found that topical application of "GABA" at the recording area produced marked changes in the voltage and polarity of those responses thought to be mediated by axodendritic synapses, and a marked increase in the voltage of the positive-wave component of the direct-projection response. Thiosemicarbazide, an inhibitor in the production of GABA, caused a striking increase of the negative-wave components of the "axondendritic" responses.

EFFECT OF NICOTINIC ACID ON THE OCULAR VESSELS OF THE DIABETIC RAT. Philip P. Ellis* and Ralph G. Janes. Depts. of Ophthalmology and Anatomy, State Univ. of Iowa, Iowa City.

Previously it has been observed in this laboratory that when the ocular vessels of severely chronic diabetic rats are injected with liquid latex these vessels usually do not fill as completely as such vessels in normal rats. Because nicotinic acid causes vasodilatation of certain peripheral vessels, this material was given to some diabetic animals before the injection of liquid latex. Diabetic rats were paired according to the duration and severity of diabetes and one half of the group was given 35 mg of nicotinic acid intraperitoneally an hour before the injection procedure. Rats were anesthetized, heparinized, and allowed to bleed through a cannula inserted into the thoracic aorta. Liquid latex was then injected at a constant pressure through the cannula which was directed cephalad. Flat mount preparations of the iris, cornea and retina were examined, and the degree of filling of the vessels in the animals that had received nicotinic acid was compared with those of their paired mates. In most instances there was better filling of the retinal vessels in the animals that had received nicotinic acid. Occasionally the limbal vessels showed more filling in the nicotinic acid treated animals but the iris vessels were usually similar in the two groups. (Supported by Grant B-237 USPHS.)

EFFECT OF CHANGE IN RENAL VEIN PRESSURE UPON RENAL VASCULAR RESISTANCE. D. Emanuel*, J. Scott*, M. Fleishman* and F. Haddy. US Army Med. Research Lab., Fort Knox, Ky.

The relationship of vein pressure to renal vascular resistance has been studied in the right kidney of 92 pentobarbitalized laparotomized dogs. Blood flow rate was maintained constant by interposing a pressure independent pump in the right renal artery. Resistance increased as a function of vein pressure, the values at 8 and 31 mm Hg being 1.01 and 1.21 mm Hg/ml/min respectively. Following extrarenal nerve section, the same vein pressure change resulted in a resistance decrease of 0.04 resistance units which was not changed by destruction of circulating catecholamines, local sympathetic nerve blockade, local parasympathetic nerve potentiation, decapsulation and dextran perfusion in live innervated or dead kidneys. At a given level of artery pressure in dextran perfused dead kidneys resistance was higher with vein pressure elevated. Elevation of artery pressure alone resulted in resistance changes which were not significantly different in innervated or denervated kidneys. Lymph flow rate from cannulated hilar vessels increased as a function of vein pressure. Winton, Swann and Gottschalk have shown that when venous pressure exceeds interstitial pressure,

both pressures rise together and are essentially equal. Gottschalk has demonstrated that a given elevation of vein pressure effects approximately equivalent changes in renal interstitial and peritubular capillary pressures. The studies of Winton, Gottschalk and Miles attest to the great rigidity of renal stroma. These observations indicate that two mechanisms control renal vascular resistance when vein pressure is changed. One accomplishes control by active vasomotion initiated by changes in non-local sympathetic nerve activity. The other passively controls resistance because stromal rigidity maintains a near constant transmural pressure with blood flow rate constant but actually decreases it with flow rate uncontrolled.

AMINO ACID CHANGES DURING KIDNEY SLICE INCUBATION IN THE PRESENCE OF THYROXINE. Nicole Etling* and S. B. Barker. Dept. of Pharmacology, Univ. of Alabama Med. Ctr., Birmingham.

Rat kidney slices were incubated in a Ringer-alanine-glucose solution as described in these proceedings by Lindsay and Barker. Chromatographic studies were carried out on the tissue and incubation media to determine any influence of thyroxine on amino acid metabolism, endogenous or exogenous, as well as any effect of added alanine or tryptophan on the metabolism of thyroxine itself. For most of the amino acids, tertiary butanol-formic acid, phenol-water or pyridine-water solvents were used and staining done with ninhydrin. During incubation, glycine, leucine, lysine and phenylalanine appeared in the medium after 24 hr, and increased in amount after 48 and 72 hr. These substances probably arose in the tissue, since they were all found there in higher concentration. The further addition of L-tryptophan did not alter the appearance of amino acids, but with D-tryptophan, leucine and lysine were absent; furthermore, a pink-yellow coloration was seen in tissues and solutions. For iodo-amino acids, butanol-ammonium hydroxide, butanol-acetic acid and methanol-ammonium acetate solvents were used. Detection of spots was done with ceric ammonium sulfate-sodium arsenite. The tissue removed up to 10 μg thyroxine/ml medium. Most of the hormone was retained as thyroxine itself, but a portion was transformed into tetraiodothyroacetic acid and some into diiodotyrosine plus iodide. The iodide was found in the incubation medium. No triiodothyronine has been detected in these experiments. (Supported by grants from American Cancer Soc. and USPHS.)

DISTRIBUTION OF I^{131} ALBUMIN IN ORGANS AND TISSUES OF THE RAT AFTER INTRAVENOUS ADMINISTRATION. N. B. Everett and B. S. Simmons*. Dept. of Anatomy, Univ. of Washington School of Medicine, Seattle.

Radioautography and conventional counter methods have been used to determine the amount and distribution of I^{131} albumin in tissues and organs of the rat following intravenous injection of the labeled compound. At 3, 30 and 60 min after injection the rats were frozen in liquid nitrogen and the organs were removed in the frozen state. Organs from several rats in each group were assayed for radioactivity which was expressed as activity per unit weight of tissue. Samples of organs from animals of each group were fixed while frozen and then processed in the routine way for radioautography. The quantitative measurements and the radioautographic observations were in agreement in revealing the following: 1) certain organs (brain, lung and spleen) showed no change in their content of labeled albumin with time; essentially all of the radioactivity in these organs was intravascular. 2) Many organs contained extravascular albumin which increased with time. The rate at which the labeled material accumulated in the tissue spaces was quite variable for the different organs in this group. The testis, intestine and skin had the greatest percentage increase. 3) The liver and adrenal evidenced a decreasing level of I^{131} albumin with time. It is suggested that these differences with respect to the organ content of I^{131} albumin relate in part to differences in vascular structure and capillary permeability. (Supported in part by Grant H-1530 from Natl. Heart Inst., USPHS.)

AVIAN PHOTOPERIODIC TESTICULAR RESPONSE AND FUNCTION OF THE HYPOTHALAMO-HYPOPHYSIAL AXIS. Donald S. Farner. Labs. of Zoophysiology, State College of Washington, Pullman.

When male White-crowned Sparrows (Zonotrichia leucophrys gambelii) receive daily photoperiods (p), 9.1 hr of continuous light of supramaximal intensity, the increase in testicular weight (W) is approximately $\log W_t = \log W_o + kt$, where t is time in days; this equation holds until W becomes about 200 mg. When p is varied between 9.1 and 17 hr the value of k for first-year birds is approximately $k = 0.009\ (p - 9.1)$. When the daily photoperiod is divided into a number of short photoperiods k becomes much larger than when the same quantity of light (p) is given as a single daily photoperiod. For example, division of p into equally spaced 50-min photoperiods results in a relationship between p and k which, although slightly curvilinear, may be represented approximately by $k = 0.009\ (p_d - 1)$, where p_d is the total daily duration of light divided into equally spaced 50-min photoperiods; this holds for p_d = ca. 4 hr to p_d = 10 hr. These results are all consistent with a hypothesis that an essential compound in the response mechanism is formed rapidly in light and disappears slowly in the dark. (Supported by Contract Nonr-1500-(00), Office of Naval Research.)

EFFECT OF PROLONGED AORTIC OBSTRUCTION ON HEMODYNAMIC AND METABOLIC FUNCTIONS IN DOGS. Enid A. Farrand*, Steven M. Horvath and Anne Everingham*. Dept. of Physiology and Cardiovascular Lab., College of Medicine, State Univ. of Iowa, Iowa City.

Occlusion of the thoracic aorta at the fourth rib interspace was accomplished in 11 mongrel dogs by means of an inflated balloon affixed to a cardiac catheter. The duration of obstruction ranged from 130 to 306 min, the average period of obstruction being 236 min. Four animals died during the obstruction period, 3 expired upon release of the occlusion, and 4 animals survived the experiment but were sacrificed or died later. All of these survivals exhibited some degree of neurological damage. Mean arterial blood pressures above the obstruction were significantly elevated during the period of occlusion and tended to fall only when death was imminent. The pressure in the aorta below the occlusion remained stable at approximately 15 mm Hg. Arterial oxygen contents and arterio-mixed venuous oxygen differences did not change significantly from control levels throughout the experiment. A marked progressive decrease in arterial and mixed venous blood carbon dioxide content occurred as a result of the occlusion. There was a significant fall in both total oxygen consumption and cardiac outout during obstruction of the aorta.

SIALOADENECTOMY AND THYROID RESPONSE TO THYROTROPHIC HORMONE. Yu-Sheng Louise Feng and Arthur W. Wase (intr. by William C. Foster). Div. of Biological Chemistry, Hahnemann Med. College, Philadelphia, Pa.

Previous observations have been reported which indicated that the salivary glands are capable of modifying thyroid activity by a reduced iodine -131 uptake, reduced turnover rate and a reduction in thyroid-stimulating hormone titer. Since sialoadenectomy imposed upon hypophysectomized rats did not result in different thyroid activities, salivary glands could act upon the thyroid in conjunction with the hypophysis or upon the hypophysis directly. In attempting to learn the mode of action of salivary gland secretion on thyroid activity, the response of a sialoadenectomized, hypophysectomized and intact animals to parenteral thyroid stimulating hormone was studied. Thyroid stimulating hormone increased the phosphorus-32 activity in the intact animal thyroids 14.2% over base-line values; in the sialex animals a 13.2% increase was observed with the 50 μg dose whereas with a 100 μg dose, a 341% was noted. Hypophysectomized animals responded to thyroid stimulating hormone in the manner expected, showing a 472% increase in phosphorus-32 activity in the thyroid. By analyzing the average weights of the thyroids a significant difference was found between the sizes of the thyroids of intact, sialoadenectomized, hypophysectomized and hypophysectomized-sialoadenectomized rats.

EFFECT OF RESERPINE ON MOTILITY OF ANEURAL SMOOTH MUSCLE. John Ferguson. Dept. of Physiology and Pharmacology, Creighton Univ. School of Medicine, Omaha, Nebr.

A study was made of the response in motility of non-innervated smooth muscle (chick amnion) to reserpine and its relationship to barium. Strips were prepared and each was suspended in 100 ml of oxygenated Sollmann-Rademaekers' solution. Records were made of motility before and after the application of the drug. Most of the preparations developed spontaneous activity. Serpasil phosphate, computed as reserpine, was added to the bath in different concentrations. Spontaneously rhythmic muscles responded to 10^{-6} by lessened activity; some were depressed by 5×10^{-7} concentration. A drop in tonus, followed by a gradually diminished amplitude and rate usually ensued after an adequate dose. Enhanced activity following stretch and release was present after reserpine but appeared to be somewhat depressed. Barium chloride in 5×10^{-6} augmented motility in rhythmic, and in 10^{-5} in non-rhythmic preparations (Am. J. Physiol. 179:635, 1954). Reserpine, when added before or after, antagonized the stimulant effect of barium. Although reserpine counteracted the effectiveness of barium, the muscle still reacted readily to histamine acid phosphate. However, reserpine appeared to diminish the excitant response to histamine but to a lesser degree than to barium. The addition to the bath of a small amount of creatinine, sodium sulfate, glucose, sodium chloride or hydrochloric acid failed to modify significantly motility in a fresh preparation. (Aided by Nebraska Heart Assoc.)

EFFECT OF DIETS HIGH IN MEAT PROTEIN ON NITROGEN METABOLISM OF THE HUMAN. Vincent Fiorica* and F. R. Steggerda. Dept. of Physiology, Univ. of Illinois, Urbana.

Three adult males were subjected to a controlled diet for 3 periods of 44 days each. In each of the periods meat protein was isocallorically added to a low nitrogen basal diet. The levels of protein in the supplemented diets were those furnished by one-half, three-quarters, and one pound of meat per day. Feces were collected in 7-day pools and urine was collected daily. Blood samples were taken for 7 consecutive days during the transition from low to high and high to low protein intakes. All samples of excreta as well as representative samples of the diet were analyzed for total nitrogen. In addition, a partition of urinary nitrogen was made in terms of ammonia, urea, uric acid, creatine and creatinine. Blood plasma was analyzed for total nitrogen, urea and non-protein nitrogen. The results of these experiments show that in each subject a marked lag in the urinary excretion of nitrogen occurs during the transition phases. Fecal nitrogen, however, remained relatively constant regardless of the changes in protein intake. In the blood, concomitant changes in urea and non-protein nitrogen parallel the urinary changes in total nitrogen during the transitions. Nitrogen balance data indicate that balance can be approximated at a protein intake furnished by one-half pound meat per day while in all subjects higher levels induce a positive balance. (Supported by grant from the Natl. Livestock and Meat Board.)

CEREBRAL BLOOD FLOW AND CEREBRAL ALCOHOL UPTAKE OF ANESTHETIZED DOGS. Ernst Fischer and Henrik Wallgren*. Dept. of Physiology, Med. College of Virginia, Richmond.

Fourteen dogs (10-24.2 kg) were given 25 mg/kg Nembutal, the cerebral blood flow (CBF) was measured by the Kety-Schmidt N_2O method and 0.4 gm/kg alcohol injected as a 10 w.% solution in saline into a femoral vein in 60-80 sec. Arterial blood samples were taken from a femoral artery, cerebral venous blood from the confluens of the sinuses by a hypodermic needle through a hole drilled in the midline of the occipital protuberance. N_2O-mixture was administered by tracheal cannula and appropriate valves. The alcohol uptake of the brain was calculated from the A-V differences of samples taken either simultaneously with the N_2O samples or immediately after the CBF determination. Blood alcohol levels were determined according to Newman and Newman. For

the 10 experiments with complete data, the mean CBF was 62.5 ml/100 gm/min (range 44.7 - 77.7). In the average, an A-V difference of 0.28 vol % was still present after 10 min and indicates some extracerebral blood in the sinus. Maximum alcohol equilibrium concentration in the brain was 140 mg % (80-245) and was reached in 85 sec (30-120) after the end of infusion. In those dogs, in which arterial alcohol concentration rose initially above 300 mg %, temporarily a high cerebral alcohol concentration was reached, and a marked outflux of alcohol occurred before final blood-brain equilibrium was established in 10-15 min. Five repeat CBFs measured 25 min after the first and 24 min after alcohol infusion were decreased 14.5% (10-19). (Aided partly by an ASLA-Fulbright fellowship to H.W.)

PERSISTENCE OF DAILY RHYTHMS IN EOSINOPHIL COUNT AND RECTAL TEMPERATURE DURING "REGRESSION" INDUCED BY INTENSIVE ELECTROSHOCK THERAPY. William Fleeson*, Bernard C. Glueck, Jr.* and Franz Halberg. Univ. of Minnesota Med. School, Minneapolis.

Does intensive electroshock therapy (REST, c.f. Psychiatric Quart., 31: 117, 1957) obliterate the 24-hr periodicity of blood eosinophils and rectal temperature, or do these daily rhythms persist during the "regression" which the treatments produce? "Regression" represents a degree of dissociation from the environment seldom seen in humans. The patients are mute, disoriented due to complete memory loss, are doubly incontinent, and show neurological changes associated with extrapyramidal tract activity. Data on 2 paranoid and 1 catatonic schizophrenic female patients were obtained. Eosinophil counts were done at 6 hourly intervals, starting 3 days before the REST, and continuing through the recovery period. Rectal temperatures were obtained at 3 hourly intervals during this same period. The data suggest that the rhythms in eosinophils and temperature persist during the "regressed" state induced by the daily administration of 2 shocks at 8 a.m. and two at 8 p.m., for 10, 11 and 12 days respectively. The results seem to indicate a degree of independence of these daily rhythms, from the cerebral cortical functions which are gravely altered, if not obliterated by REST. No evidence was obtained fro the induction of a 12 hourly periodicity in either rhythm, despite the continuance of the 12 hourly shock schedule for more than a week.

EFFECT OF CHANGE IN RENAL VEIN PRESSURE UPON URINE FLOW RATE. M. Fleishman*, J. Scott*, D. Emanuel*, and F. Haddy. US Army Med. Research Lab., Fort Knox, Ky.

The effect of variation in vein pressure through venous obstruction upon urine flow rate has been studied in the right kidney of 104 pentobarbitalized laparotomized dogs. Urine flow rate decreased as a function of vein pressure, the value at 28 mm Hg being 60% of that at 8 mm Hg. The percentage decrease appeared to be less in kidneys infused with drugs which prevent an active intrarenal resistance increase (Circ. Res. 4: 659, 1956). In contrast to the studies of Winton, steady state urine flow rate with both vein and ureter pressures elevated to 20 mm Hg was not different from that with vein or ureter pressure elevated alone. When blood flow rate was maintained constant elevation of vein pressure as high as 50 mm Hg failed to change urine flow rate. Lymph flow rate from cannulated hilar lymph vessels increased as a function of vein pressure but protein concentration remained unchanged. Gottschalk has shown that approximately equal changes in the levels of interstitial pressure, intratubular pressure and peritubular capillary pressure occur following venous obstruction; Winton and Selkurt that glomerular filtration and blood flow rates decrease; Winton that tubular reabsorption is likely unchanged, and Winton that glomerular filtration rate is not changed if blood flow rate be maintained constant. These observations indicate that, as a result of stromal rigidity, filtering surface and effective filtration pressure do not change greatly following vein pressure elevation with blood flow rate constant. They also indicate that the reduction in urine flow rate following venous obstruction likely is related to a reduction in blood flow rate resulting from a resistance increase, decreased arterial transmural pressure and active intraenal constriction.

HYPOTHALAMIC HYPERPHAGIA IN PARABIOTIC RATS. David G. Fleming (intr. by O. O. Stoland). Dept. of Physiology, Univ. of Kansas, Kansas City.

The phenomenon of hyperphagia resulting from bilateral destruction of the ventral medial nucleus of the hypothalamus was investigated in the parabiotic rat. Animals parabiosed at 21 days by the Bunster-Meyer method were allowed to mature until the age of 3 months. Bilateral lesions were then placed in the ventral medial nucleus of one member of the pair. A pronounced hyperphagia developed in the animal with the lesion causing a rapid increase in the body weight of the pair. An average increase of 215 gm was seen within 30 days. The marked disparity in size between the right and left animal established that most of the gain was confined to the rat with the lesion. A second group of parabiotic animals was conditioned to partitioned cage feeding. In this manner it was possible to determine individual food intake. Preoperatively both members of the pair had essentially identical food consumption. After the lesions were placed, however, there was an immediate increase in the food intake of the operated animal followed by a gradual decrease in the food intake of the intact partner until its food consumption was 25% below the preoperative level. These animals also showed major increases in body weight. This experiment lends additional support to the hypothesis that humoral agents are released into the systemic circulation as a result of eating and that they play a role in the control of food intake. In addition, the intact member of a parabiotic pair does not prevent the appearance of hyperphagia in its partner when the latter has been subjected to hypothalamic damage.

RADIOACTIVE IODIDE TRANSFER ACROSS THE RAT STOMACH IN THE DIFFUSION CELL. William C. Foster and Bernard P. Lewis*. Dept. of Physiology, Hahnemann Med. College, Philadelphia, Pa.

The transfer of carrier-free radioactive sodium iodide across the rat stomach was studied in an in vitro system. The stomachs of fasted adult Wistar-strain rats were extipated and separated into the peptic and mucous gland portions. These tissues were then stretched between the chambers of a modified Delrue diffusion apparatus. Tyrode's solution was placed on the nutrient side of the membrane and 2 microcuries of radio-active sodium iodide in water on the lumen side. The apparatus was placed in waterbath at 37°C and a CO_2 - O_2 mixture bubbled into the diffusion cells. Samples of 0.2 ml volume were removed from both cells at 1/2 hr intervals for a period of 2 hr and the radioactivity determined. Only 0.069-0.34% of the radioactive iodide crossed the gastric membranes in the 2-hr period. This transfer appeared to be enhanced by histamine and partially blocked by iodoacetic acid. (Supported by Grant H-1588, Natl. Heart Inst., USPHS.)

CONTINUOUS RECORDING OF CARDIAC OUTPUT BY A CONSTANT-RATE INJECTION DYE-DILUTION TECHNIC. Irwin J. Fox*, and Earl H. Wood. Mayo Fndn. and Mayo Clinic, Rochester, Minn.

Development of a dye detectable in whole blood independent of variations in oxygen saturation (Fed. Proc. 16: 39, 1957) has made possible application of dilution technics to the venous circulation. Known concentrations of tricarbocyanine dye II were injected at a constant rate through a cardiac cathether (#6F) into the pulmonary artery in 8 anesthetized dogs breathing 100% oxygen. The resulting indicator dilution was recorded continuously by cuvette oximeters from a femoral artery and the right ventricular outflow tract (via a second #7F cardiac catheter). With injection into the pulmonary artery only recirculating indicator reaches the right ventricle, so that concentrations recorded at the femoral artery can be corrected for recirculated dye by use of the concentrations recorded from the right ventricle as a baseline and allowing for the time difference between these sampling sites. Cardiac output can be determined continuously as long as injection and sampling are continued. In 6 determinations cardiac output values over a 1-min period varied ±9% from the mean value and differed by 9 and 17% from values obtained from neighboring instantaneous T-1824 curves and direct Fick procedures. The average time difference between

the femoral and ventricular sampling sites was 9 sec. Varying the time correction between sampling sites by ±2 sec altered the output values by only 4%. The effects on systemic output of respiration, injections of epinephrine and norepinephrine and induction and resuscitation from ventricular fibrillation were studied.

EFFECT OF ACUTE PULMONARY VASCULAR HYPERTENSION ON TRANSPULMONARY PRESSURE IN EXCISED CAT-LUNGS. N. R. Frank (intr. by W. H. Forbes). Dept. of Physiology, Harvard School of Public Health, Boston, Mass.

The purpose of this study was to determine whether the effect of acute pulmonary vascular congestion on lung volume is influenced by the degree of lung distension at which vascular congestion occurs. The static volume-pressure curve of 9 excised cat-lungs was measured during deflation following inflation to an airway pressure of 20 cm H_2O; left auricular pressure was maintained at -3 cm H_2O. Lung volume was then kept constant at identical points on the static elastic curve, and changes in airway pressure were measured while pulmonary congestion was induced. To induce congestion, left auricular pressure was raised from -3 cm H_2O to 30 cm H_2O, being maintained at that level about 10 sec. Changes in transpulmonary pressure were minimal, or did not occur, at lung volumes in the range of functional residual capacity (FRC). Above the FRC there was an increase in transpulmonary pressure in response to vascular hypertension, which became progressively greater at larger lung volumes. (At a transpulmonary pressure of 15 cm H_2O, the average increase was 2.2±1.0 cm H_2O.) At lung volumes smaller than the FRC, transpulmonary pressure was reduced by vascular hypertension. (At zero transpulmonary pressure, the average decrease was 0.4±0.2 cm H_2O.) The findings are interpreted as evidence that acute pulmonary vascular hypertension increases elastic recoil of excised lungs when lung volumes are larger than the FRC, has little or no effect on elastic recoil at or near the FRC, and acts to reduce elastic recoil at smaller volumes. (Aided by grant from Natl. Fndn. Infantile Paralysis.)

PULMONARY VASOMOTION AS INFLUENCED BY PULMONARY BLOOD TEMPERATURE. Pierre-M. Galletti* and Peter F. Salisbury. Inst. for Med. Research, Cedars of Lebanon Hosp., Los Angeles, Calif.

The systemic and pulmonary vascular beds have been perfused separately with constant minute volumes (Salisbury et al., Circulation Res. 5:303, 1957). Special care was taken to avoid hemolysis and embolic phenomena, and to maintain pH, oxygenation and temperatures in both circulations at physiological values by continuous monitoring and adequate corrections. While the factors known to influence pulmonary vasomotion were kept constant, the temperature of the blood circulating through the lungs was varied in discrete steps between 15° and 40°C. Significant changes of pulmonary arterial and venous pressures were observed. The calculated pulmonary resistance increased from 3 to 21% for each diminution of 1°C, and varied conversely with increases in temperature. A temperature of 40°C caused a steady and irreversible increase of pulmonary venous pressure with secondary elevation of pulmonary arterial pressure. The pressure-flow relationship was studied over a wide range of perfusion rates at different temperatures. Attempts were made to evaluate the relative contribution of pulmonary vasomotion, changes of blood viscosity and pseudoplastic properties of the blood.

EFFECTS OF SCHIZOPHRENIC SERA, LSD 25, AND SEROTONIN ON TISSUE CULTURES OF BRAIN CELLS. R. S. Geiger (intr. by Percival Bailey). Research Labs., Neurophsychiatric Inst., Univ. of Illinois, College of Medicine, Chicago.

In vitro cultures of human cerebral cortex react to sera from schizophrenic patients with marked morphological changes. These patients were not receiving drugs. During the first 2 days the Nissl substance gradually aggregates and also concentrates around the nuclear membrane. These aggregates subsequently break up and diffuse throughout the cytoplasm by the 6th-10th day. During this

period some dendrites flatten out, others retract. These changes alter the characteristic appearance of the neuron. There effects are partly similar to some observed previously with LSD 25 and with serotonin. LSD 25 (0.001 gamma/ml) causes the Nissl substance to diffuse as with schizophrenic sera, but this change occurs within 20 min. The nucleus increases in density and the nucleolus increases markedly in size and motility, spreads to the margin of the nucleus indicating production of nucleoprotein. Prolonged exposure to LSD 25 causes vacuolization of the cytoplasm and dissolution of Nissl substance. Serotonin (1 gamma/ml - 5 gamma/ml) also aggregates Nissl substance within 10 min. After 3 hr exposure to serotonin some staining properties of the nucleoplasm change and within 2-3 days the neurons degenerate. Serotonin causes a slow rhythmical pumping movement in the neurons not observed with the other 2 agents described above. Glial motility is either unaffected or accelerated by schizophrenic sera, but is reduced on addition of serotonin or LSD 25.

OXYGEN COST OF CARDIAC HEMODYNAMIC ACTIVITY. A. Gerola*, H. Feinberg* and L. N. Katz. Cardiovascular Dept., Med. Research Inst., Michael Reese Hosp., Chicago, Ill.

The development of a preparation for measuring total coronary flow in a relatively intact dog has been used to investigate the determinants of coronary flow. Studies have been accomplished with controlled variations of blood pressure, cardiac output, heart rate, arterial oxygen and carbon dioxide content, pH, and with catecholamine administration. Findings support the concept that coronary flow is determined primarily by the metabolic cost of hemodynamic activity. Blood pressure (BP) and heart rate (HR) are important determinants of oxygen consumption. Variations in cardiac output (CO) show no consistent correlation with cardiac oxygen consumption (O_2C). The usual calculation of cardiac work (W)—i.e. the product CO × BP—gives no weight to HR, an important determinant of cardiac oxygen consumption. Further, it emphasizes CO, a component having no correlation with oxygen consumption. Therefore "efficiency," (W/O_2C), is an index only of the oxygen cost of the external work performed by the heart and not of the oxygen cost of hemodynamic cardiac activity. The product, HR × BP was calculated, as an index of the repetitive development of tension by the cardiac muscle, in a variety of conditions. This product correlated more closely with oxygen consumption than the HR or BP individually. Regression curves of oxygen consumption plotted against BP × HR were calculated and a comparison was made, for hypoxemic dogs, with regression curves of oxygen consumption plotted against efficiency. The latter yielded a relative decreasing O_2 requirement with increasing external work in mild and severe hypoxemia. The plot, HR × BP, revealed a constant relationship under control, mild and severe hypoxemic conditions. It would appear, then, that the product BP × HR is a better index for the oxygen cost of cardiac hemodynamic activity.

CONTINUOUS CROSS-TRANSFUSION BETWEEN IRRADIATED AND NON-IRRADIATED RABBITS. Herbert B. Gerstner and Phillips M. Brooks*. Dept. of Radiobiology, School of Aviation Medicine, USAF, Randolph AFB, Texas.

X-radiation of 900 r induced in rabbits circulatory collapse within 2 hr following exposure. Cross-transfusion was performed between irradiated and nonirradiated animals to study whether or not this collapse was mediated by a blood-borne chemical factor. Cross-transfusion started at 30 min prior to irradiation, continued throughout the exposure time of 30 min, and ended 3 hr following irradiation. With the exchange rate used—6 cc of blood/min/animal—the following results were obtained: first, in the irradiated partner circulatory collapse occurred at the same time and to the same degree as in animals that received irradiation but no transfusion; second, in the nonirradiated partner circulation remained normal as judged by the constancy of blood pressure, pulse amplitude and heart rate. Therefore, as far as the initial blood pressure reaction was concerned, a protective effect of the nonirradiated on the irradiated partner could not be demonstrated; a damaging influence of the irradiated on the nonirradiated partner likewise could not be found.

INNERVATION OF THE URETHRA. J. M. Girado*, J. Husby*, and J. B. Campbell* (intr. by Walter S. Root). Dept. of Neurological Surgery, College of Physicians and Surgeons, Columbia Univ., New York City.

Functional analysis of the autonomic innervation of the urethra is obtained in decerebrate succinylcholinated female cats by delivery of electrical stimuli to the distal ends of the hypogastric or pelvic nerves. The bladders are closed at the ureteral and urethral vesicle junctions and cannulated via the dome. The proximal end of the severed urethras remain open. Urethral resistance is gauged by rate of flow of saline from a catheter introduced from the outside to a point just proximal to the external sphincter. Simultaneous manometric recordings are obtained from both catheters. The bladder contracts in response to either pelvic or hypogastric nerve stimulation. The urethra relaxes 3-4 sec following the onset of bladder contraction in response to pelvic nerve stimulation. The simultaneous contraction of both organs results from hypogastric nerve stimulation which is followed by a period of urethral relaxation. The use of autonomic drugs indicates that the urethra received inhibitory fibers from the pelvic nerve and both excitatory and inhibitory fibers from the hypogastric. These data elucidate the innervation of the urethra, emphasize the significance of the sympathetic nervous system in micturition, and indicate the reciprocal relationship of the urethra to the bladder in this function. (Supported by Dept. of the Army, Office of the Surgeon-General, Playtex Park Research Inst. and United Cerebral Palsy Assocs., Inc.)

CARDIAC ENERGETICS OF ACUTE ARTERIOVENOUS FISTULAE IN DOGS. Vincent V. Glaviano and Florian Nykiel (intr. by W. V. Whitehorn). Univ. of Illinois College of Medicine, Chicago.

The cardiac alterations resulting from varied-size artificial fistulae of the femoral vessels were investigated in 12 anesthetized open-chest dogs. The mean blood pressure and the cardiac minute volume and coronary sinus flow were continuously recorded, the latter 2 measurements were made with electromagnetic rotameters. The arteriovenous oxygen difference of the left ventricle was determined from oxygen analysis of arterial and coronary sinus blood during bouts of open A-V fistula of 5 min duration. Following a control period, during which time pressure and flows were allowed to stabilize, the sudden opening of a large unilateral fistula was followed by an immediate decrease in blood pressure and coronary sinus flow, with a concurrent increase in cardiac output. In a short period of time the coronary flow established at a level independent of the percentage decrease or increase in blood pressure and cardiac output respectively. The left ventricular work and the oxygen consumption determined near the end of the 5-min period was found to be elevated above control. Occlusion of the fistula reversed the direction of the measured parameters to control values.

EXPERIMENTAL STUDY OF THE PATHOGENESIS OF PAPILLEDEMA. William B. Glew*, Thomas P. Kearn*, C. Wilbur Rucker* and Hiram E. Essex. Mayo Clinic and Mayo Fndn., Rochester, Minn.

Pathogenesis of papilledema is still a controversial subject. Though clinical and pathological studies have provided valuable information, elucidation of the basic pathophysiology of this sign requires controlled animal experimentation. The production of papilledema in experimental animals has been reported. However, a method for repeatedly producing papilledema in animals analagous to that seen in man has not been evolved. The objective of this study has been to clarify the pathogenesis through such animal experimentation. Since papilledema in man is most frequently bilateral and associated with intracranial disease, investigation was directed toward the production of papilledema by simulating intracranial disease. Such attempts to produce papilledema in the dog were uniformly unsuccessful. The production of papilledema was accomplished in long term experiments in 2 of 6 monkeys by the gradual inflation of a subdural balloon. The ocular fundi were photographed demonstrating bilateral papilledema after inflation of the balloon and normal optic discs in the same monkey several

weeks after deflation of the balloon. The papilledema photographed resembles closely papilledema observed in man both in appearance and in the slow rate of development and subsidence. A comparison of the intracranial pressures and necropsy findings failed to account for the production of papilledema in 2 monkeys, but not in the others. The determination of the crucial factors in the production of this papilledema must therefore await further investigation.

HYPOKALEMIA AND RESPIRATORY ALKALOSIS IN ANESTHETIZED DOGS DURING ACUTE DECOMPRESSION STRESS. Armand J. Gold*, Frederick P. Ferguson and Jeanne Q. Barry*. Dept. of Physiology, Univ. of Maryland School of Medicine, Baltimore.

The hypothesis that respiratory alkalosis is a factor in producing hypokalemia during acute exposure to moderate decompression stress has been examined. Dogs were anesthetized with sodium pentobarbital, placed in a decompression chamber and subjected to a simulated altitude of 30,000 ft (225.6 mm Hg) for 30 min. Arterial blood samples were obtained 1-4 min prior to, and at the end of 5, 15 and 30 min of decompression. In one group of 14 experiments, the animals breathed room air throughout the procedure. The mean plasma K^+ concentration fell from a predecompression level of $3.91 \pm .07$ mEq/l. to $3.44 \pm .10$ mEq/l. after 30 min at 30,000 ft, a decrease of 0.47 mEq/l. A marked rise in blood pH and fall in arterial pCO_2 occurred, indicating a respiratory alkalosis. In a second group of 15 experiments, the dogs breathed a gas mixture containing 20% CO_2, 21% O_2 and 59% N_2 during the decompression phase. The concentration of CO_2 was equivalent to 45 mm Hg pressure at 30,000 ft. Under these conditions, respiratory alkalosis was prevented and the characteristic hypokalemic response failed to occur. It is therefore concluded that respiratory alkalosis constitutes an important factor in the production of hypokalemia during acute decompression stress. The precise mechanism by which alkalosis and hypokalemia are related remains somewhat obscure. Potassium may leave the plasma and move intracellularly as a possible compensatory response to alkalosis.

THYROID AND GASTRIC ACID SECRETION IN THE ANESTHETIZED RAT. Dale Goldsmith* and E. S. Nasset. Dept. of Physiology, Univ. of Rochester School of Medicine and Dentistry, Rochester, N. Y.

Saline was perfused thru the stomach of an anesthetized rat and pH of the effluent measured every 5 min. The pH remained at 5.5-6.0 in normal, unstimulated, control rats. After i.v. injection of methacholine the pH decreased 0.6-1.6 units in 14 of 19 control animals; in the remaining 5 control rats the pH changes never exceeded 0.6 units, and the free acid liberated after stimulation was less than 1/3 that liberated by the responsive group. In 23 rats fed desiccated thyroid or its fractions, only 6 showed the larger acid output characteristic of responsive controls after methacholine stimulation; the remaining 17 animals gave pH changes similar to unresponsive controls. The feeding of desiccated thyroid to rats, therefore, reduces their ability to secrete free gastric acid after methacholine injection. About 65% of desiccated thyroid dissolves in water at pH 6.4. On acidification of the extract to pH 4.6, 70% of the dissolved material precipitates. This fraction, which contains most of the activity, does not dialyze. The material in desiccated thyroid which causes inhibition of gastric acid secretion appears, therefore, to be associated with colloidal substances. Since the active material is absorbed from the gastrointestinal tract it is probably not a large molecule.

SPREAD OF EPILEPTOID ACTIVITY THROUGH BRAINSTEM AND RHINENCEPHALON IN THE CAT, WITH SPECIAL REFERENCE TO THE HYPOTHALAMUS. Elsie F. Goodfellow, William T. Niemer and Ervin W. Powell (intr. by C. M. Wilhelmj). Dept. of Anatomy, Creighton Univ. School of Medicine, Omaha, Nebr.

Numerous subcortical structures were stimulated electrically, at a constant parameter of stimulation, and the electrical activity of the hypothalamus was recorded for each point stimulated. Sites most epileptogenic for the

hypothalamus were found to be: most areas of the rhinencephalon; lateral posterior nucleus, pulvinar and lateral geniculate body of the thalamus; and the brachium of the inferior colliculus, the superior colliculus and central grey of the midbrain. Rhinencephalic structures were the most positive. Subsequently, the abnormal electrical activity of other areas of the subcortex was studied in conjunction with that of the hypothalamus following stimulation of rhinencephalic structures such as the amygdala, septum and hippocampus. In this survey, widespread abnormal electrical activity prevailed throughout the subcortex, according to the area stimulated; e.g. stimulation of the basal medial amygdala led to increased activity in most subcortical areas. Activity of an ictal nature with synchrony and high amplitude was recorded from the hypothalamus and from various thalamic nuclei, particularly the pulvinar and dorsomedial nuclei. Stimulation of the hippocampus and septum likewise caused diffuse spread of abnormal activity through the subcortex. Simultaneously with the EEG activity, blood pressure and gastric motility were recorded. Stimulation of the basal medial amygdala caused a rise in blood pressure and a decrease in gastric motility during the period of abnormal electrical activity. Septal stimulation slightly raised the blood pressure, but stimulation of the hippocampus had no apparent effect. (Aided by USPHS Grant B.1046.)

SUPPRESSION OF TOXIC AND PHYSIOLOGIC ACTIONS OF THE ADRENALINES BY SEROTONIN. Paul Gordon, John J. Robinson and Morris A. Lipton (intr. by F. J. Haddy). VA Research Hosp. and Dept. of Pharmacology, Northwestern Univ. Med. School, Chicago, Ill.

Our laboratory has shown that serotonin is capable of depressing the mortality of mice given bacterial endotoxin. It is well established that endotoxin administration is followed by a secretion of and hypersensitivity to the adrenalines, with the ultimate development of shock and death. As anti-adrenergic drugs have been effective in the pretreatment of endotoxin and other forms of shock, the possibility that serotonin might prove to be a natural anti-adrenergic compound was investigated. Serotonin was found to possess anti-adrenaline and anti-noradrenaline activity in both toxicologic and physiologic experiments: 1) pretreatment with serotonin markedly delayed and, with increase in dose, ultimately reduced the mortality of mice given an intravenous LD_{100} dose of adrenaline or noradrenaline. This protection was already prominent at 120 gamma/24-gm mouse and at 1.3 mg/mouse afforded a permanent survival of 70%. Lung weights were equally elevated in both groups; however, the lungs, heart and kidneys of the controls were hyperemic and hemmorhagic while the organs of the treated group were not. 2) Serotonin pretreatment at -5 min suppressed the pilomotor response of mice to the IM injection of adrenaline or noradrenaline, placement on a cold plate, and the injection of reserpine; the relationship of these findings to the sympathetic nervous system will be discussed. 3) In rabbits the hyperglycemic response to 0.1 mg/kg subcutaneous adrenaline was lowered to less than half by the simultaneous administration of 0.9 mg/kg serotonin, divided between the subcutaneous and intraperitoneal routes.

MULTIPLE TIME CONCENTRATION CURVES IN URINE AND RENAL VENOUS BLOOD AFTER RAPID INJECTION INTO THE RENAL ARTERY. Irving Green and Jin Min Soo (intr. by Philip Dow). Dept. Physiology, Med. College of Georgia, Augusta.

The theory that cells and plasma circulate through different renal channels and the significance of reportedly low intrarenal hematocrit ratio were investigated. The ureter, and after heparinization, the renal vein, were cannulated in situ. Renal vein blood was drained past a T-tube and into the jugular. One ml of a suspension of red cells in an isosmotic solution of T-1824, creatinine, inulin and PAH was injected into the renal artery instantaneously and without disturbing flow. The whole renal vein flow was diverted with samples taken every half second. Heart rate, blood pressure, renal blood flow (agreeing with measured flow), extraction of PAH, inulin, and creatinine indicated normal renal and cardiovascular function. Dilution curves of cells and plasma had identical

shape and detailed land marks not only with each other but with curves from the kerosene perfused kidney reported elsewhere. Small time differences, attributed to laminar flow were not excluded but the mean circulation time of plasma av. 5.0 sec and cells av. 4.7 sec plainly exclude the possibility that the hematocrit ratio of the actively circulating blood can be half that of the shed blood and lead to the conclusion that low organ hematocrit ratios seen in the literature must be due to extravascular or sequestrated plasma (see abstract by Soo and Green in this program). From a cardiovascular research training program supported by American Heart Association and the United States Public Health Service (HTS 5044).

BIOCHEMICAL CHANGES OF THE BLOOD OF MAN DURING EXERCISE. James Green, Bruno Balke and Jerry Lowe (intr. by Robert T. Clark). Dept. of Physiology-Biophysics, School of Aviation Medicine, USAF, Randolph AFB, Texas.

Human subjects were exercised on either the treadmill or the electrically controlled bicycle ergometer. Two tests which varied in time from 15 to 24 or 90 min were used to exercise the subject. The long-term exercise was maintained at a work load which would give a constant pulse rate of 140 to 150 beats/min. The short-term studies were accomplished by varying the intensity of the work each minute until a pulse of 180 was attained. The average time to reach 180 pulse was 14.5 min. Those individuals lasting 20-24 min were in excellent physical condition. During the experiment, an indwelling needle was placed in the ante cubital vein to permit periodic withdrawal of blood. In the 90-min exercise period blood was taken at 0 time, then at time intervals for 90 min, whereas, in the graded work blood was drawn at 0 time, then when 120, 140, 160, and 180 pulse was attained. The blood was analyzed for various constituents, including cholesterol, amino acid nitrogen, ketone bodies, blood sugar and lactic acid. In the 90-min experiment, lactic acid rose for about 20 min then began to fall toward the resting level. The better the physical condition, the more rapid this fall. In the graded studies the lactic acid rose in a tri-phasic curve. In all studies, the cholesterol rose sharply during the first 12-20 min.

RHINENCEPHALIC LESIONS AND SEX BEHAVIOR IN CATS. J. D. Green, C. D. Clemente and J. de Groot*. Univ. of California at Los Angeles, School of Medicine, and VA Hosp., Los Angeles.

Electrolytic or surgical lesions were placed in the amygdala, piriform cortex or hippocampus of 83 out of 122 cats. The remaining cats were used as controls for behavior, weight increase and the behavioral effects of castration and gonadal steroids. Hypersexuality in males was correlated with lesions in an area of the piriform cortex. Hyperphagia was found to occur with lesions near the junction of the lateral and basal amygdaloid nuclei. Catatonic and unreactive ("placid") behavior followed lesions in the rostral amygdala. "Fearful" or "aggressive" behavior was associated with seizures and followed hippocampal injury. The latter was at times observed to occur following the production of small lesions in the amygdala or piriform cortex, apparently due to occlusion of the hippocampal blood supply from local edema. In the controls it was found that estrus behavior or increased male drive could be induced hormonally without corresponding changes in the reproductive tract or secondary sex characteristics. Differences between adult and prepubertal responses were also seen.

RELATION OF CHANGES IN CONCENTRATION OF CERTAIN ELECTROLYTES TO CONDUCTION AND REPETITIVE RESPONSES IN THE TURTLE VENTRICLE. William Richard Green* and Sheppard M. Walker. Univ. of Louisville School of Medicine, Louisville, Ky.

Ventricular strips were prepared to demonstrate the action of normal Ringer's solution, potassium ions and calcium ions on conductivity and on the production of repetitive responses in cardiac muscle. Electrodes were arranged for stimulation and recording at the ends of the strips. An electroencephalograph was used to record electrical responses. After the strips are soaked in normal

Ringer's, conduction is normal and no ectopic beats occur. After soaking in K-rich Ringer's, conduction is generally delayed or stopped, and ectopic beats seldom occur. When the preparation is subsequently soaked in normal Ringer's, the threshold usually decreases, conduction velocity greatly increases, and in some cases repetitive responses occur. However, in other cases, no repetitive responses occur until after the 2nd or 3rd soaking in normal Ringer's. Repetitive responses were consistenly elicited after treatment with normal Ringer's subsequent to a second treatment in K-rich Ringer's. After soaking the preparation in a solution of one-half isotonic calcium chloride and one-half normal Ringer's, the conduction velocity is decreased. With a second treatment in the Ca-rich solution, the conduction velocity is slowed further or blocked completely. Muscle pretreated with Ca-rich solution usually showed lowered threshold and increased conduction velocity when resoaked in normal Ringer's. Under these conditions series of repetitive responses were elicitable at both ends of the ventricular strip. (Supported grant H-697(C7) from the Natl. Heart Inst., USPHS, and by the Kentucky Heart Assoc.)

RADIOACTIVITY OF GASTRIC JUICE SECRETED IN RESPONSE TO C^{14} HISTAMINE. Morton I. Grossman and Edward R. Woodward*. VA Ctr. and Univ. of California Med. Ctr., Los Angeles.

Histamine dihydrochloride labeled with C^{14} in the 2 position of the ring was given subcutaneously to 7 dogs with Heidenhain pouches. The dose was 1 mg with an activity of 42 μc. Samples of blood serum and gastric juice were collected at intervals after injection and their radioactivity was measured. Radioactivity is expressed in terms of micrograms of histamine base although it is realized that some of the activity may be in metabolites of histamine. Serum activity reached a peak of from 56 to 110 μg/l. in from 15 to 30 min and then slowly declined so that at 2 hr it was still more than 50% of the peak value. The initial samples of gastric juice, collected before peak secretory rates had been reached, had the lowest radioactivity, ranging from 3.1 to 7.4 μg/l. Maximum concentration of radioactivity varied from 10.2 to 35.5 μg/l. and occurred in samples collected after the peak rate of acid secretion had passed. The ratio of radioactivity to acid secreted varied both within and between dogs. Minimum values were 0.03-0.09 μg of histamine base per mEq of acid secreted and maximums were 0.06-0.25. There was no consistent pattern relating these ratios to rate of acid secretion.

CHANGES IN PLASMA FIBRINOLYTIC ENZYME COMPONENTS FOLLOWING PARENTERAL TRYPSIN. M. Mason Guest and D. R. Celander*. Depts. of Physiology and Biochemistry, Univ. of Texas Med. Branch, Galveston.

Crystalline trypsin, 20-300 mg/dog, dissolved in 0.9% saline, was introduced by the intramuscular, intravenous and intra-arterial routes. As much as 300 mg of trypsin introduced into the skeletal muscle of the leg in acute experiments failed to produce overt whole blood fibrinolytic activity or significant changes in the Lee-White clotting time, fibrinogen, profibrinolysin, prokinase, antifibrinolysin or latent coagulable protein. In contrast, 50% or more of the animals exhibited frank fibrinolysis when crystalline trypsin, 5-10 mg/kg, was given by either vein or artery over a period of 10-20 min. Concomitant with the appearance of fibrinolysis in whole blood samples, significant decreases occurred in plasma fibrinogen, latent coagulable protein, profibrinolysin, antifibrinolysin and prokinase. In many cases the Lee-White clotting times were markedly prolonged and only soft clots were formed, if clotting did occur. The in vivo fibrinolytic activity continued to be manifest for several hours. However, in experiments in which the animal was heparinized before the injection of trypsin, frank fibrinolytic activity did not develop.

MECHANISM OF THE INCREASE ARTERIAL PRESSURE CAUSED BY EPINEPHRINE INJECTION. Arthur C. Guyton, Arthur W. Lindsey*, Berry

Abernathy* and Jimmy B. Langston*. Dept. of Physiology and Biophysics, Univ. of Mississippi Med. Ctr., Jackson.

The mechanism by which epinephrine increases the arterial pressure has been investigated in 11 dogs. The blood flow was shunted from the right atrium through an external flow meter and then back into the pulmonary artery, and total spinal anesthesia was instituted to block all autonomic nerve impulses. Infusion of epinephrine at a rate of 0.0035 mg/kg/min increased the total peripheral resistance a mean of 78%, the cardiac output 151%, the arterial pressure 351% and the mean circulatory pressure 205%. At lower rates of infusion, the results were essentially the same though of proportionately less magnitude. It is obvious, therefore, that the increase in arterial pressure was caused principally by increased cardiac output rather than by increased total peripheral resistance. Since cardiac output is greatly dependent on the mean circulatory pressure (Physiol. Rev. 35:123, 1955), the primary cause of the increased cardiac output, and hence also of the increased arterial pressure, was found to be increased mean circulatory pressure. Epinephrine increases the mean circulatory pressure by increasing the general vasomotor tone throughout the circulation. This often occurs with very little or no actual constriction of vessels, which seems to have been the case in these experiments for it was mainly increased mean circulatory pressure rather than increased total peripheral resistance that caused the arterial pressure to rise. (Aided by grant from the Natl. Heart Institute, USPHS.)

EFFECT OF CHANGE IN BLOOD FLOW RATE UPON RENAL VASCULAR RESISTANCE. F. Haddy, D. Emanuel*, J. Scott*, and M. Fleishman*. US Army Med. Research Lab., Fort Knox, Ky.

The effect of changing flow rate in the range 25-180 ml/min upon renal vascular resistance has been studied in 82 pentobarbitalized laparotomized dogs. Flow rate was varied with a pressure independent pump interposed in the right renal artery. Resistance decreased as a function of blood flow rate with rates between 25 and 75 ml/min and increased with rates between 75 and 180 ml/min. However, intra and interindividual comparisons showed the onset of the resistance increase to be flow rate independent but pressure dependent. The onset was observed at all flow rates from 25 to 180 ml/min in kidneys of approximately the same size and failed to occur even at the highest flow rate in low resistance kidneys not developing arterial pressures exceeding approximately 80 mm Hg. In some kidneys a resistance increase was observed at one time but not at another and was related to the initial level of resistance. The onset occurred at mean arterial pressures between 50 and 100 mm Hg, the value being remarkably constant in a given kidney. The above relationships were unchanged by extrinsic nerve section, destruction of circulating catecholamines, local sympathetic nerve blockade, local parasympathetic nerve potentiation, increased CO_2 tension and H^+ and decapsulation. The resistance increase was abolished and replaced by a progressive resistance decrease during blood perfusion by intermittently using dextran as the perfusate, during dextran perfusion and during blood perfusion in dead kidneys. Elevation of arterial pressure by increasing blood flow rate failed to significantly increase lymph flow rate from cannulated hilar lymph vessels. Winton, Gottschalk, Swann and Miles have shown that arterial transmural pressure increases as a function of artery pressure. These observations indicate that the resistance increase results from active vasoconstriction due to a direct effect upon vascular smooth muscle of an increase in arterial transmural pressure.

RENAL EXCRETION OF RADIOIODIDE IN THE RAT. N. S. Halmi and R. G. Stuelke (intr. by R. G. Janes). Dept. of Anatomy, State Univ. of Iowa, Iowa City.

Rats were injected with 2 ml/100 gm body weight of water or various solutions (154 mEq/1. of sodium chloride, choline chloride, sodium thiosulfate, sodium perchlorate or stable sodium iodide; isotonic saccharose), 12 mg of propylthiouracil and a tracer dose of radioiodide. Renal excretion of radioiodide was

assessed by several criteria (U/P_I131, % dose excreted in 1 and 5 hr, clearance), and was found to be enhanced in the animals given chlorides, perchlorate or stable iodide. In these rats U/P_I131 ratios were between 1.9 and 21.1, whereas in the other groups they were often below 0.5 (minimum: 0.12). Comparison of groups treated with various substances showed no correlation between ioduresis and urine flow. The mechanisms implicated in renal tubular reabsorption of radioiodide in man and dogs (passive diffusion modified by ionic interactions) do not appear to be the only ones operating in rats. Rather, an active transport system which can be saturated with iodide and possibly competitively inhibited by related anions also seems to play a role. (Supported by grant A-932, USPHS.)

LEUKOCYTE RESPONSE TO CARDIOVASCULAR CATHETERIZATION. Lyle H. Hamilton. Univ. of Saskatchewan, Wood VA Hosp. and Marquette Univ. School of Medicine, Milwaukee, Wis.

During cardiac catheterization studies on dogs, a consistent pattern of changes in the circulating leukocyte count was observed. The initial change was a dramatic panleukocytopenia, which was maximal after 1-2 hr. After 4-5 hr a relative and absolute neutrophilia developed, characterized by a shift to the left. Eosinophil and mononuclear cell levels gradually increased to the control values. The pattern of response appeared to be independent of the route of catheterization, the final position of the catheter or the duration of the procedure. The response did not occur after simple ligation and incision of veins without introduction of a cardiac catheter.

EFFECTS OF COLD EXPOSURE ON THE OXIDATIVE METABOLISM OF RAT LIVER HOMOGENATES. John P. Hannon (intr. by Kaare Rodahl). Dept. of Biochemistry, Arctic Aeromed. Lab., Ladd AFB, Alaska.

Since very little has been reported concerning the intermediary metabolic processes leading to the high in vitro respiratory rate of liver tissue in the cold exposed rat, the oxidative metabolism of various metabolites by liver homogenates was studied. Animals were exposed to 5±1°C for 29-33 days before use. The metabolites included: lactate, citrate, isocitrate, α-ketoglutarate, succinate, fumarate, malate, glutamate and β-hydroxybutyrate. Endogenous respiration was measured. The endogenous respiration of the tissue as well as catabolism of all of the substrates studied, with the exception of lactate, was found to be significantly higher in the cold exposed animal than in the control animal. No change was observed in lactate oxidation. Two levels of respiratory increase were noted in the results: the first amounting to 18-21% was found in the case of citrate, fumarate, malate and glutamate and the second, amounting to 29-39% was found in the case of isocitrate, α-ketoglutarate, succinate and β-hydroxybutyrate. Tissue from cold exposed animals using succinate substrates had a high initial rate of oxygen consumption which fell sharply after 10 min incubation. Controls, however, fell gradually during the entire incubation period. Differences in cold exposed tissue response were also noted using other substrates. These findings indicate that cold exposure leads to some undetermined derangement of the enzyme systems responsible for the oxidation of the substrates mentioned.

EXPLANATION OF THE EFFECT OF TUBE SIZE ON THE VISCOSITY OF BLOOD. Robert H. Haynes* and Alan C. Burton. Department of Biophysics, Univ. of Western Ontario, London.

Fahråeus and Lindqvist (Am. J. Physiol. 96:562, 1931) were the first to observe that the apparent viscosity of blood at high shear rates is smaller when measured in tubes of very small diameter than in large tubes. The phenomenon can be explained on the basis of a theory due to Dix and Scott Blair (J. Appl. Physiol. 11:574, 1940) which predicts an enhanced flow in small tubes over that expected on the basis of Poiseuille's law. The relative increase in the flow rate, which is responsible for the fall in apparent viscosity, can be attributed to the finite size of the red cells which becomes a significant fraction of the diameter of the small tubes. Mathematically, this means that the flow rate from the tube

must be calculated by a summation procedure rather than an integration. It is also possible to calculate the "asymptotic" viscosity in a tube of infinite diameter and the "effective" size of the red cells from the theory. The authors have verified the applicability of the theory from the available data in the literature as well as from their own measurements made in connection with an extended investigation of the rheology of blood. The essential idea of the theory can be presented in such a simple way as to warrant its inclusion in undergraduate physiology courses when the Fahrâeus-Lindqvist effect is discussed. (Supported by grant from Life Insurance Med. Research Fund.)

DIETARY CARBOHYDRATE AND BILE VOLUME FLOW IN RAT. Franklin W. Heggeness (intr. by Wallace O. Fenn). Dept. of Physiology, Univ. of Rochester School of Medicine and Dentistry, Rochester, N. Y.

Improved calcium utilization is observed when lactose or galactose is incorporated into the diet of rats. A decreased excretion of calcium in the various secretions into the gastrointestinal tract could account for a part of this effect. As one of these secretions bile flow was measured in the rat following administration of these and other carbohydrates. The bile duct was cannulated and flow measured in the fasting state and following intravenous and oral administration of several carbohydrates. By either route galactose administration at dosages of 1 mg or more/gm of body weight was followed by a prompt sustained decrease in flow. The percentage decrease and duration of effect are in proportion to dosage administered. When protein is fed along with galactose the depression is less marked. To a lesser extent lactose also depresses flow, while fructose, glucose and several pentoses studied do not. Calcium excretion is greater at high as compared to low flow rates.

PULMONARY FUNCTION AFTER SPINAL TRANSECTIONS IN MAN. Allan Hemingway and Ernest Bors*. Univ. of California School of Medicine at Los Angeles and Long Beach VA Hosp., Los Angeles.

From the large group of paraplegic patients 3 groups of subjects were selected for physiological investigation of pulmonary function. The patients were chosen based on completeness of the spinal lesion causing paralysis and loss of sensation in all segments innervated from below the lesion. The 3 groups were: 1) spinal lesions in the lumbar region; 2) spinal lesions in the thoracic region; 3) spinal lesions in the lower cervical region. The patients of group 1 had normal innervation of all respiratory muscles except those of the lower abdomen and pelvic floor musculature. The patients of group 2 were breathing only with chest muscles and diaphragm, while those of group 3 were using only the diaphragm and accessory muscles. A normal control group of subjects were given the same tests (except blood gases) of respiration. Measurements were made of vital capacity and component volumes, maximum breathing capacity, residual volume, arterial blood gases and respiratory metabolism during a weight lifting exercise test. The patients of group 1 had pulmonary function which differed insignificantly from normal. The patients of group 3 who were using the diaphragm as their only effective muscle of respiration had surprisingly efficient respiration considering their loss of functional respiratory musculature. Their vital capacity was approximately 70% of the normal control group while the maximum breathing capacity was approximately 55% of normal. Results for group 2 were intermediate between groups 1 and 3. In the mild exercise test the oxygen consumption rate was only approximately 2.5 times the basal value, no insufficiency in breathing occurred. Apparently diaphragmatic breathing is adequate for respiration in paraplegics. This does not provide, however, any expiratory force for coughing.

POTASSIUM AND SODIUM MOVEMENTS IN THE EHRLICH MOUSE ASCITES TUMOR CELL. Harold G. Hempling (intr. by R. F. Pitts). Dept. of Physiology, Cornell Univ. Med. College, New York City.

Studies have been conducted on the movements of sodium and potassium into and out of the Ehrlich ascites tumor cell. Under steady state conditions, at 22°C,

in the absence of an exogenous source of glucose, the cell flux for both potassium and sodium averaged 0.8 $\mu M/10^7$ cells/hr or 3.0 $pM/cm^2/sec$. The cell can accumulate potassium and extrude sodium against electrochemical gradients for both ions. It is possible under the experimental conditions reported to separate the transport systems for these 2 ions. Thus, it has been shown that under conditions of low temperature with a diminished metabolism, net fluxes for the 2 ions are different. Also, following periods of 24 hr at 2°C, an exogenous source of glucose enhances the accumulation of potassium 7-fold while sodium extrusion is uninfluenced by the presence of glucose. Similarly, potassium exchange rates are temperature dependent, with Q_{10} values as high as 5, while exchange rates for sodium are temperature insensitive, with Q_{10} values of 1.2-1.6. Glycolysis has been eliminated as an energy source for the transport processes since these processes go on in the absence of an exogenous source of glucose. It is estimated that a maximum of 4% of the energy derived from the total oxidative metabolism of glucose would be required to support independent transport of potassium and sodium.

EFFECT OF HORSE SERUM ON THE TOTAL EOSINOPHIL AND WHITE CELL COUNT OF THE ALBINO RAT. D. Henry* and E. Da Costa. Chicago Teachers College, Chicago, Ill.

A study of the effect of dextran and horse serum injections on the total eosinophil and white cell counts of 25 male and 21 female rats was made. In a 2-month-old dextran injected group, total eosinophils in the males were reduced from the pre-injection level of 58-16 and 28 after the 5th and 6th weekly injections. In the females, the only reduction occurred after the 1st injection. In 2-1/2-month-old males injected with horse serum, the total eosinophils rose from the pre-injection count of 96-175 after the 6th injection. In females, the eosinophils rose from 74-95 after the 3rd injection. In a 14-month-old group injected with horse serum, the eosinophils rose steadily in the males after each injection from 116 to 400. In the females, the eosinophils rose from 133 to 716 after the 3rd injection but were 200 after the 6th. The total white cells in both males and females increased after the 2nd injection and continued with fluctuations through the 6th. The rats therefore responded to foreign protein by a rise in eosinophils but showed no other symptoms of sensitivity. The dextran group showed a decrease in eosinophils with attendant symptoms of stress.

ULTRASONIC FLOWMETER: EXPERIMENTAL TESTS OF RELIABILITY. J. F. Herrick, Joseph A. Anderson* and Hiram E. Essex. Sections of Biophysics and Biophysical Research and Physiology, Mayo Clinic and Mayo Fndn., Rochester, Minn.

The reliability of the ultrasonic flowmeter when measuring the flow of blood through artifical circulatory systems has been established. In vivo calibrations have been made using various direct methods whereby the actual volume of flow is known, The satisfactory performance of the ultrasonic flowmeter depends on as thorough an appreciation as possible of the propagation characteristics of ultrasound. A fundamental requisite for accurate measurements is the transmission of the signal through the moving liquid. All other signals (ultrasonic energy propagated by other routes) must be suppressed. The method permits continuous and quantitative display of velocity changes throughout the cardiac cycle. If backflow is present, it may be observed quantitatively. A photograph of the flowmeter's response to backflow which was produced deliberately by artifical methods will be shown. The ultrasonic method of measuring blood flow requires special technics for determining the zero position of the velocity indicators. Two independent methods have been developed for determining the zero position when measuring the flow of blood through artifical circulatory systems. Only one of these methods can be used when we begin to measure blood flow in vivo.

CLEARANCE OF POTASSIUM IN THE DOG. R. C. Herrin. Dept. of Physiology, Univ. of Wisconsin Med. School, Madison.

Infusion of $NaHCO_3$ in 3 dogs increased the clearance of K 10 to 18 times and the clearance of citric acid 21 to 25 times. After chronic daily administration of KCl, the infusion of KCl at a rate of 24 mg/min in 3 dogs, of about 20 kg elevated the ratio of the clearances of K to creatinine to 0.68 - 0.78 with the exception of one period of 1.05. The clearance of citric acid was not elevated. In 2 dogs adrenal cortical extract did not elevate this ratio. One dog died about 22 hours after the plasma K was 5.8 mEq/1, during the last clearance period. Its post-mortem plasma K was 20.0 mEq/1. This suggests that cortical extract had depressed adrenal cortical function. After an interlude, K administration in combination with meat feeding was again tried. Infusion of KCl at 24 mg/min elevated the ratio to 0.70; at 42 mg/min it rose to 1.11 and then fell to 0.94; after resumption of 24 mg/min, it rose to 1.13. In other tests higher infusion rates sometimes depressed the ratio. During the KCl infusion the clearance of creatinine rose markedly.

ACCELERATION OF THE GROWTH RATE OF THE FRUIT FLY LARVA DURING CONTINUAL CENTRIFUGATION. William F. Herrin and Charles C. Wunder (intr. by G. Edgar Folk, Jr.). Dept. of Physiology, State Univ. of Iowa, Iowa City.

Newly hatched Drosophila Melanogaster larvae can be centrifuged continuously at fields of 200-1000 times the earth's gravity with no marked effect upon either the growth rate or the final size. Extrapolation of data from higher fields as well as results with other forms suggested that the growth rate might increase under these conditions. An index of growth rate is obtained by evaluating the rate constant in the Verhulst-Pearl equation fit to the average daily size of groups of animals under observation. It is found that this equation fits the course of growth for these animals while they are maintained at a constant field. It has been reported that the growth rates of these larvae subjected to fields between 1000 and 5000 times the earth's gravity suffer a decrease which is roughly linear with respect to field intensity. (Wunder, C. G., Proc. Soc. Exper. Biol. & Med. 89:544, 1955.) The results obtained at less than 1000 times gravity seem at variance with the simple relations obtained at the higher fields. A possible explanation for these results is to consider the interplay of the increased work which must be done by the animal in transporting metabolic materials against gravitational attraction and the physiological adjustments made to compensate for this need.

HEMATOENCEPHALIC EXCHANGE AND NEUROLOGICAL MATURATION. Williamina A. Himwich and JoAnn C. Petersen*. Thudichum Psychiatric Research Lab., Galesburg State Research Hosp., Galesburg, Ill.

The free glutamic acid level of the brain is approximately 60 mg% for the newborn of both rabbit and cat in contrast to values of about 120 and 150 mg% respectively in the adult animal. The amount increases slowly until after the first month of life when it approaches that of the adult. The development of the so-called blood-brain barrier has been studied in the young of these species by injecting intraperitoneally 2 gm/kg of L-glutamic acid as sodium glutamate at pH 7.0. The whole brain, removed 30 min later, was analyzed for free glutamic acid. An increase in this amino acid over values of the control animals is taken to mean that glutamic acid has passed from blood to brain. Using this criterion as well as the occurrence of convulsions, Himwich and Petersen (Neurology, in press) have shown that the penetration of glutamic acid into the rat brain decreases markedly between the 10th and 17th days of life. The newborn rat not only shows a great increase in free glutamic acid in brain but also convulses strongly when glutamic acid is administered as described above. In contrast to the rat, newborn kittens and rabbits do not convulse, and the free glutamate in brain shows no significant increase. These data suggest that the rabbit and cat are born more mature, in terms of the blood-brain barrier, than is the rat.

DEFINITION OF THRESHOLD FOR THE CONDITIONED AUDITORY GALVANIC SKIN RESPONSE. J. E. Hind and A. E. Aronson (intr. by C. N. Woolsey). Depts. of Physiology and Speech, Univ. of Wisconsin, Madison.

Forty college students with normal hearing were conditioned by pairing 40% shock reinforcement with a 1000 cps tone 10 db above their voluntary thresholds. The GSR was recorded as a conductance change on a cathode ray oscilloscope with the sweep synchronized with the tone onset. After conditioning, a random pattern of test tones was presented which included 8 tones (5 unreinforced) at each of 5 intensities: +10, +5, 0, -5 and -10 db re voluntary threshold. Orderly relations were found between tone intensity and mean GSR amplitudes and latencies. Significantly stronger conditioning was noted for subjects exposed to tones of 0.6 sec duration than for durations of 3.0 sec. On the basis of the uniform distribution of latencies and low amplitudes at -10 db the responses at this intensity are interpreted as spontaneous (unrelated to tone). By assuming that the frequency of spontaneous response at -10 db will occur at all intensities on those trials lacking a true response, the number of responses observed at each intensity has been corrected for spontaneous activity. By making use of the relation between stimulus intensity and central tendencies of the amplitude-latency collection for all subjects, criteria for "true" responses have been defined which yield thresholds in good agreement with the voluntary threshold when applied to the responses of each individual. (Aided by the Alfred Laukhuff Trust, the Natl. Inst. of Neurological Diseases and Blindness (B-896) USPHS, and the Research Committee of the Univ. of Wisconsin.)

SOMATIC AFFERENT AREA I OF THE CEREBRAL CORTEX OF CEBUS. Jean François Hirsch and William S. Coxe (intr. by C. N. Woolsey). Lab. of Neurophysiology, Dept. of Physiology, Med. School, Univ. of Wisconsin, Madison.

The postcentral receiving area was mapped in 9 individuals for the purpose of comparing development of the localization pattern in this animal, which possesses a tail of moderate prehensile ability with the pattern in Ateles, in which the functions of this appendage are much more highly elaborated. In the latter animal marked development of the tail area with the extension onto the dorsal surface of the hemisphere is associated with shift of the leg and arm areas lateralward in the postcentral gyrus and an almost complete displacement of the face area from a postcentral into a precentral position around the lower end of the central sulcus and into the Sylvian fissure. These modifications are accompanied by gross changes in the fissural pattern. In Cebus the tail area is longer than in Macaca but much smaller than in Ateles. The leg area still occupies part of the medial wall but the face area lies largely anteriorly below the end of the central sulcus. The gross morphological features of interest are a broad precentral gyrus and fusion of the inferior temporal and Sylvian sulci at their confluence, perhaps a result of a lateral shift of the parietal lobe. This shift is less than in Ateles, since the intraparietal sulcus which fuses with the Sylvian in Ateles, is still present. In some experiments, responses to light pressure stimuli were evoked in the precentral agranular cortex. (Supported by grant B-732 Natl. Inst. of Neurological Diseases and Blindness, USPHS.)

RQ OF ARCTIC ANIMALS. Raymond J. Hock. Arctic Aeromed. Lab., Ladd AFB, Alaska.

Studies on metabolic rate of Arctic mammals and birds have been reported (Scholander et al, Biol. Bull. 99:237, 1951). RQ's derived from this study do not vary in relation to greatly reduced temperature (from 40° to -40°C), as has been reported for other stresses such as muscular exercise. RQ of animals found: lemming, 6 records, 0.735 average (range, .71 to .76); least weasel, 89, .721 (.65 to .82); Eskimo dog, 70, .752 (.65-.90); Arctic fox, 98, .742 (.65-.86); polar bear cubs, 56, .806 (.67-1.02); domestic pigeon, 40, .829 (.67-1.09); Alaska jay, 10, .738 (.65-.90); glaucous gull, 45, .713 (.65-.83); snow bunting, 207, .753 (.65-1.05). A few values below 0.65 have been discarded, but for most species RQ indicates that fat is major fuel of combustion, despite food ingested as protein or carbohydrate. No evidence of high RQ during fat deposition was found, as Erikson (Acta Scand. Physiol. 36:75, 1956) has reported for Arctic ground squirrel. Since increased activity of muscles results in varied RQ, lack of

variation of RQ in relation to cold may indicate that heat production may come from other sources than muscles.

CHEMICAL COMPOSITION OF NATIVE CANINE GASTRIC MUCUS. Franklin Hollander and Ruth C. Rubin*. Gastroenterology Research Lab., Mount Sinai Hosp., New York City.

The literature contains no information on the chemical composition of relatively pure native gastric mucus secretion. Accordingly, measurements have been made on a variety of chemical constituents and related factors in 6 pooled specimens of acid-free mucus, collected from canine gastric pouches following the topical application of acetylcholine solution by the technique previously reported from this laboratory. The present report will include data on the content of organic, inorganic and total solids; hexosamine; carbohydrate, non-carbohydrate and total reducing power; protein, non-protein and total nitrogen. In addition to values for concentrations of these constituents—expressed as μg or μM/μg of secretion, and also per μg of organic solids—data will be presented concerning various molecular ratios derived from these concentration values. Concentration per unit volume of secretion was abandoned because of the high viscosity of the mucus and consequent errors in volume measurements. Electrolyte concentration data for the formulation of a "chemical anatomy diagram" of this variety of mucus will also be presented. (Supported by grant C-288 from the Natl. Cancer Inst., USPHS.)

UTILIZATION OF BLOOD UREA IN RUMINANTS. T. R. Houpt (intr. by F. H. McCutcheon). Dept. of Physiology and Pharmacology, School of Veterinary Medicine, Univ. of Pennsylvania, Philadelphia.

Schmidt-Nielsen et al. (Am. J. Physiol. 188:477, 1957) report utilization of injected urea in the camel, presumably through the protein synthetic action of rumen microflora. This finding was confirmed and extended, and the pathway of urea transfer from blood to rumen investigated, using sheep as experimental ruminants. First, 2 young, mature ewes were placed upon a low-protein ration, carbohydrate supplemented, insufficient to maintain body weight. This favored rumen microbial protein synthesis and retention of synthesized protein, and produced a low basal urea excretion rate. Urea was injected intravenously (ca. 5 mmol urea-N/kg body weight), and, in part, recovered as the excess over basal urea excretion rate, calculated from control rates. 52% (S. D. = 10%) of injected urea was retained, i.e. "utilized." Measurement of post-injection decline in body urea content and of urinary urea excretion indicated a disappearance rate of 10 mmols urea-N/hr (S. D. = 3 mmols/hr). Without carbohydrate supplement retention of injected urea decreased to 22% (S. D. = 5%). Secondly, in acute experiments the rumen-reticulum cavity was isolated from adjacent parts of the digestive tract, the ingesta was replaced with physiological saline, and accumulation of ammonia-N, representing a hydrolytic product of urea was measured. Simultaneous absorption of ammonia-N was estimated from arteriovenous urea and ammonia concentration data. Secretion of urea-N in saliva was also determined. Under these conditions total urea-N transfer rate, the sum of ammonia-N accumulation and absorption plus salivary urea-N, for four sheep was 5.2 mmols urea-N/hr (S. D. = 0.8 mmols/hr), of which 0.3 mmols/hr was in saliva.

CARDIAC OUTPUT STUDIES ON 245 DOGS. Charles D. Howell*, E. Allbaugh Farrand* and Steven M. Horvath. Depts. of Biology and Physiology, Univ. of Redlands and State Univ. of Iowa, Iowa City.

The Fick principle was used to calculate the cardiac outputs. Arterial and venous blood samples were obtained by catheterization from 6 sites which gave these cardiac outputs (l/min) I) aorta-pulmonary artery, 2.32± 0.85; II) femoral artery - right auricle, 2.55 ± 0.67; III) femoral artery-pulmonary artery, 2.38 ± 0.79; IV) femoral artery-right ventricle, 2.26 ± 0.79; V) left ventricle-right ventricle, 2.67 ± 0.94; VI) aorta-right ventricle, 2.35 ± 0.64; the mean of the entire series was 2.36 ± 0.77. Statistical studies were made of the arteriovenous oxygen difference, oxygen consumption, heart rate and systolic pressure.

Applications of the t-test revealed a number of significant differences, usually between extremes of the 6 groups. However, physiological explanation for these deviations was not apparent. Heart rate and systolic pressure appear to be at least as variable as cardiac output. A subsequent study of cardiac outputs at intervals over a 4-hr period immediately after Nembutal anesthesia suggested that cardiac outputs were highly variable for about the first 2 hr, and then attained a lower level which was less variable in the succeeding 2 hr.

INFLUENCE OF VARYING DEGREES OF "PASSIVE" LIMB MOVEMENTS UPON RESPIRATION AND OXYGEN CONSUMPTION OF MAN. B. K. Hutt*, Steven M. Horvath and G. B. Spurr. Dept. of Physiology and Cardio-vascular Lab., State Univ. of Iowa, Iowa City.

Measurements of gaseous exchange were carried out during 17 experiments on 10 adult male subjects. One, 3 or 6 joints were passively moved at a constant rate of 20/min in each subject. A rest period of at least 30 min preceded each of these manipulations. Oxygen consumption, carbon dioxide production, minute ventilatory volume and respiratory rate were measured continuously. A 26% increase in ventilatory minute volume occurred consequent to passive movement of a single joint with no change in oxygen consumption. Movement of 3 or 6 joints produced further increases in minute volume but were accompanied by similarly significant elevations in oxygen consumption. Apparently peak responses were obtained following movements of 3 joints. The significance of these observations in relationship to theories of respiratory control will be considered.

THYROXINE EXCRETION INCREASE BY COLD EXPOSURE. A. Intoccia* and L. Van Middlesworth. Dept. of Physiology, Univ. of Tennessee, Memphis.

Six albino rats were maintained at 12°C and 6 controls at 22°C. After 24 days, 10 mg $KClO_4$ were injected intraperitoneally to block the thyroid glands. One hour after $KClO_4$, each rat was injected intraperitoneally with 1.6 μg I^{131} thyroxine and the excreta collected. Twenty-four hr after I^{131} thyroxine injection, the cold-exposed rats excreted 7 times more fecal I^{131} than controls (31% of dose vs. 4%). The differences were less pronounced during succeeding days, as the I^{131} pools were depleted. Food consumption of the cold-exposed rats was double that of controls, their fecal mass was proportionately greater. It has been reported that rats exposed to cold increase their dietary intake, thyroid weight and thyroxine requirement. The data of these experiments suggest that the increased thyroxine requirement of cold-exposed rats may be due partly to an increase in thyroxine loss via the feces.

EFFECT OF FEEDING ON THE C^{14}-HISTAMINE CONTENT OF THE GLANDULAR STOMACH AND SMALL INTESTINE OF THE RAT. A. C. Ivy and Richard W. Schayer. Dept. of Clin. Science, Univ. of Illinois College of Medicine, and the Rheumatic Fever Research Inst., Chicago.

Twenty-four rats were withdrawn from food for 14-20 hr then injected with C^{14}-L-histidine. From 32 to 42 hr later 12 of the rats were fed and 12 were not fed over an additional period of from 18 to 30 hr. Feeding decreased the amount of C^{14}-histamine in the glandular stomach to the average extent of 52% and in the small intestine to the extent of 30%.

EFFECT OF ADMINISTRATION OF GLUCOSE AND GALACTOSE ON BLOOD AND AQUEOUS HUMOR LEVELS IN NORMAL AND DIABETIC RABBITS. Ralph G. Janes and H. W. Lichtenberger*. Dept. of Anatomy, State Univ. of Iowa, Iowa City.

Since galactose is a cataractogenic substance, a comparison has been made of the quantitative distribution of glucose and galactose in normal and diabetic rabbits. Levels of these sugars in the aqueous humor and blood have been determined. Galactose was separated from glucose by glucose oxidase. Fifteen gm of glucose or galactose were given intraperitoneally during a 10-min period and sugar levels were determined 20 min after this injection. Before these monosaccharides were given the ratio of aqueous to blood sugar levels was 1.10±0.04

for both normal and diabetic animals. The aqueous humor glucose levels were greater than the blood sugar levels in 95% of these control samples when the glucose was determined by the Somogyi technique. However, after glucose was administered the ratio was 0.75±0.03 for the normals and 0.90±0.03 for the diabetics. The ratios of total reducing substances following the galactose injection were 0.70±0.03 for normals and 0.87±0.02 for the diabetics. In the galactose treated normal rabbits, 43% of the total reducing substance in the blood was galactose. In the diabetics there was only 24%. Galactose in the aqueous of the normals, on the other hand, was 37% and 15% for the diabetics. Of the actual galactose administered, however, more was recovered from the aqueous of diabetics than of normals. Glucose and galactose tolerance tests for blood and aqueous of normal and diabetic rabbits will be presented. Under the conditions of these experiments, there appears to be no great difference between the concentration of administered glucose and galactose in blood and aqueous humor of the rabbit. (Supported by Grant B-273 USPHS.)

FORM OF THE MOTOR-UNIT ACTION POTENTIAL. L. W. Jarcho, C. L. Vera*, P. M. Williams*, and C. G. McCarthy*. Dept. of Medicine, Univ. of Utah College of Medicine and VA Hosp., Salt Lake City.

When skeletal muscle is activated voluntarily the electromyogram consists of a series of motor-unit potentials. In the clinic the form of these potentials is used as an aid in the differential diagnosis of diseases affecting muscle. The usefulness of the method is limited because of uncertainty regarding the normal degree of variation in the forms seen. Factors determining motor-unit form were studied in the gracilis anterior of the rat. The muscle was exposed in situ and its surface explored with both monopolar and bipolar electrodes during reflex activation. Records taken at millimeter intervals showed marked variation in motor-unit potential form in different areas of the muscle, including polyphasic types commonly regarded as evidence of disease. The factors responsible for these appearances were investigated. The most important determinant of potential form was the spatial relation of the recording electrodes to the active end-plates. Temporal dispersion resulting from differences in propagation rate among fibers of one unit and interdigitation of units both tended to increase the complexity of wave form. The effect of variation in interelectrode distance was also studied. Confirmatory observations of fibrillary activity in denervated muscle indicated that even single fiber potentials commonly produce polyphasic records. (Supported by Grant #B-446, Natl. Inst. of Neurological Diseases and Blindness, USPHS.)

TROPHIC NERVE EFFECTS WITHOUT FUNCTIONAL CONTINUITY. N. C. Jefferson*, T. Ogawa* and H. Necheles. Dept. of Gastrointestinal Research, Michael Reese Hosp., Chicago, Ill.

We have shown that, in the dog, when one phrenic is cut and immediately anastomosed, the diaphragm remains paralyzed for 3 months; yet, it shows no evidence of atrophy. Simultaneous controls with exeresis of the phrenic showed generalized atrophy of the diaphragm. Further observations demonstrate: response of the anastomosed phrenic occurs first below the anastomosis in 6 - 7, above the anastomosis in 10 -11 wk. This applies not only to the phrenics; when a proximal vagus is anastomosed to a distal phrenic the diaphragm does not degenerate, and vagus stimulation produces diaphragmatic contraction in 12 wk. The response of an organ appears to be specific to it, independent of which nerves are anastomosed, as demonstrated by contraction of the diaphragm or stomach upon nerve stimulation above the anastomosis. With phrenicophrenic and with vagophrenic anastomosis, relatively rapid return of response after 3 months; with phrenicovagal anastomosis, slow return of response (stomach) after 20 months. Conclusions: in an anastomosed nerve the response to stimulation appears first below the anastomosis rather than above. The phrenic is not unique in its ability to maintain trophic influence on the diaphragm; the vagus can play the same role. Organ response is specific, independent of the anastomosed nerve. Trophic effects of the anastomosed nerves are maintained

in the absence of function of the diaphragm for 6 wk, and in the absence of response of the diaphragm to stimulation above or below the anastomosis.

CHANGES IN INTESTINAL WEIGHT DURING HEMORRHAGIC SHOCK. Paul C. Johnson* and E. E. Selkurt. Dept. of Physiology, Western Reserve Univ. School of Medicine, Cleveland, Ohio.

Seventeen mongrel dogs anesthetized with sodium pentobarbital were employed in this study. Shock was induced by bleeding to 55 mm Hg for 90 min followed by further bleeding to 35 mm Hg until the animal began to take up blood from the reservoir. Changes in intestinal weight were determined by separating an intestinal segment of about 70 gm weight, keeping vascular supply and innervation intact. The segment was wrapped in moist gauze, enclosed in a plastic container and suspended from a beam balance. Weight changes were recorded by an optical manometer connected to the balance by a tambour system. Control experiments showed no significant alterations in intestinal weight over a period of 6-8 hr. Bleeding caused a decrease of intestinal weight in two-thirds of the shock experiments, while an increase occurred in the remainder. This increase in weight was seen in about 50% of the experiments in the duodenum and the jejunum, but was not seen in the ileum. With reinfusion of blood the intestinal weight returned toward control levels. Thirty min after reinfusion the mean intestinal weight was 100.1±11.8% of control. When the animal was well into the irreversible shock state (MABP = 60 mm Hg), the mean intestinal weight was 107.7±16.0% of control. The mean changes cited above would amount to 0.5 and 38.5 gm respectively for the entire small intestine. These experiments indicate that pooling of blood or extravascular fluid in the intestine is not responsible for the circulatory collapse observed in hemorrhagic shock.

SIMULTANEOUS MEASUREMENTS OF PULMONARY CAPILLARY BLOOD FLOW AND BLOOD VOLUME, TISSUE VOLUME AND DIFFUSING CAPACITY IN MAN. R. L. Johnson, Jr.*, W. S. Spicer*, J. M. Bishop* and R. E. Forster. Dept. of Physiology and Pharmacology, Grad. School of Medicine, Univ. of Pennsylvania, Philadelphia.

We have developed a breath-holding technique for simultaneously measuring pulmonary capillary blood flow ($\dot{Q}_C$) and blood volume (V_C), tissue volume (V_T) and diffusing capacity (D_L). It consists of making a single inspiration of a gas mixture containing approximately 0.4% CO, 0.5% acetylene, and 10% helium in various combinations of oxygen and nitrogen; this breath is held for a measured time after which an alveolar sample is collected and analyzed. As previously reported D_L and V_C may be determined from the rate of disappearance of CO in reference to helium at different levels of alevolar oxygen concentration; $\dot{Q}_C$ and V_T may be determined from the rate of disappearance of acetylene in reference to helium. Four normal subjects were studied at rest, during exercise and during Valsalva maneuvers. In an individual subject D_L and $\dot{Q}_C$ were linearly related as were V_C and $\dot{Q}_C$ in the 2 subjects in which V_C was measured. The average values of $\dot{Q}_C$ during Valsalva, at rest, and at the highest level of exercise were 3260, 5960 and 14000 ml/min respectively; corresponding values of D_L were 21, 26, and 44 ml/(min x mm Hg) respectively. These preliminary data suggest that the increase in V_C which accompanies an increase in $\dot{Q}_C$ is predominantly the result of opening up new capillaries, rather than the distension of capillaries previously patent.

EFFECT OF COLD ACCLIMATIZATION ON SHIVERING AND NON-SHIVERING THERMOGENESIS. D. R. Johnston, T. R. A. Davis and F. C. Bell (intr. by J. R. Blair). U. S. Army Med. Research Lab., Fort Knox, Ky.

Two fractions of thermogenesis due to cold exposure have been demonstrated in the rat by the use of diathermy and curare. It was further demonstrated that the fraction elicited by substitution with diathermic irradiation was of a non-shivering nature and that the fraction elicited by substitution with curare administration was due to shivering. These studies indicated that shivering was regulated by the effect of cold on skin receptors and that the non-shivering

thermogenesis appeared to be regulated by central temperature changes. The present study was designed to determine the role of these 2 thermogenic fractions during acclimatization to cold using the known effects of curare upon muscle; the central temperature effects of diathermy; the combined effects of both; and the direct measurement of shivering activity by integrating the muscle action potentials obtained by means of electromyography. Shivering activity decreased and disappeared completely at 15 days in the Sprague Dawley rats and in 25 days in Wistar survivors. This disappearance of shivering has previously been reported. The effect of curarization upon total oxygen consumption gradually diminished until 40 days when little effect, if any, could be demonstrated. The combination of curare and diathermy showed that as the duration of exposure increased an unknown 3rd fraction occurred which eventually fully replaced the thermogenic fraction of shivering in every respect in that it was regulated by the effect of cold on skin receptors.

TONOMETRIC CHECKS ON CALCULATED VALUES OF CO_2 TENSION IN URINE AND PLASMA. John T. Kaim*, Gaspar Carrasquer*, Robert Shapiro* and William A. Brodsky. Depts. of Physiology and Chemistry, Univ. of Louisville, Ky.

Previous reports on calculated values of CO_2 tension indicated that significant gradients between urine and plasma existed under conditions of metabolic acidosis and alkalosis, and of respiratory acidosis. We became skeptical of the validity of such calculations because they led to the unconventional inference that the tubule wall must present a barrier to diffusion of CO_2. Tonometric determinations were made on standard solutions, and on specimens of urine and plasma of dogs. Values, so obtained, for pK' and α CO_2 agreed to within 1% of those reported by Van Slyke on standard solutions. Determinations of α CO_2 and pK' were made on the urine and plasma of a lactic-acid loaded dog. These biological fluids were equilibrated at 38°C with gases of varying, but known CO_2 tensions. Values of α and pK so determined in urine and plasma agreed to within 1% of those usually used. Thus, pCO_2 values calculated with tonometrically determined constants were not measurably different from those calculated with assumed constants. This helps establish the validity of calculated values of CO_2 tension in urine and plasma, particularly under conditions of acidosis. Herein, the pH of both fluids lies in a range favorable for valid application of the Henderson-Hasselbalch equation. In conclusion, tonometric checks have not eliminated the existence of pCO_2 gradients, even when pCO_2 of urine is less than that of plasma.

CARDIAC PHYSIOLOGY OF THE SCORPION, PALAMNAEUS BENGALENSIS. M. S. Kanungo (intr. by R. E. Johnson). Dept. of Zoology, Ravenshaw College, Cuttack, India, and Physiology Dept., Univ. of Illinois, Chicago.

Isolated and in situ heart preparations of the scorpion, Palamnaeus bengalensis show autonomous rhythmicity with contractions developing simultaneously throughout the myocardium. The rate of heart beat is 54-62/min at room temperature (26°C). In isolated preparations the rate of beat is slightly higher than that of in situ preparations indicating regulatory effect of the alary muscles. The heart is insensitive to chloroform and to half saturated and fully saturated ether. Acetylcholine more concentrated than 5×10^{-5} depresses the heart rate. Most hearts show a reduction in amplitude, rest-pauses and sporadic irregularities in these concentrations. A tolerance to acetylcholine up to 10^{-4} is observed if the hearts are previously treated with more dilute solution of the drug. Physostigmine potentiates the effect of acetylcholine, but has no effect on the heart by itself. Histamine (10^{-4}) and adrenaline (10^{-4}) accelerate the heart rate and their effects are reversible. Histamine antagonizes acetylcholine action and hearts depressed by acetylcholine can be revived by this drug. All depressed hearts revive quickly if washed with warm saline. In view of the above studies and due to the presence of a dorsal chain of ganglia on the heart (Police, 1902), it is concluded that the pacemaker of the scorpion heart is of the innervated myogenic type in contrast to the neurogenic pacemakers of the hearts of Limulus

and spiders. Thus in Arachnida the hearts are of various types as in Insecta and Crustacea, and have no taxonomic relationship. (Supported by a grant from the Government of Orissa, India.)

EFFECT OF DIETARY STEARIC ACID ON ROOSTER LIVER STEROL. Esko Karvinen* and T. M. Lin. Dept. of Clin. Science, Univ. of Illinois College of Medicine, Chicago.

Stearic and palmitic acid have been shown to augment fecal sterol elimination (Am. J. Physiol. 187:173, 1956). In the present work, the response of sterol biosynthesis to stearic acid feeding was evaluated in 4 groups of 5 roosters on isocaloric diets. Group I was given mash only. Group II received mash with 10% stearic acid. Group III received mash supplemented with 1% cholesterol. Group IV received both stearic acid and cholesterol. Incorporation of intraperitoneal sodium acetate-1-C^{14} in liver sterol was determined in vivo. The following relative radioactivities were recovered in liver sterol: group I, 88 cpm; group II, 208 cpm; group III, 19 cpm; and group IV, 21 cpm/total liver digitonide. The respective amounts of total liver sterol were 184, 150, 723 and 850 mg/rooster. It is concluded that depletion of body sterol by stearic acid feeding was compensated by an increased biosynthesis of sterol. Administration of dietary cholesterol blocked hepatic biosynthesis of sterol and the blockade was not alleviated by stearic acid feeding.

CHANGES IN RETICULAR FORMATION THRESHOLDS UNDER ALTERED HORMONAL CONDITIONS IN THE RABBIT. M. Kawakami* and Charles H. Sawyer. Univ. of California at Los Angeles and VA Hosp., Long Beach.

In the estrous rabbit exogenous progesterone initially elevates the degree of behavioral estrus and reduces the threshold of reflexogenic release of pituitary ovulating hormone. Twenty-four hr later these conditions are reversed (Fed. Proc. 11:138, 1952) and progesterone has generally been considered an inhibitor of estrus and ovulation in the rabbit. Seeking neural correlates of these neuroendocrine fluctuations we have measured thresholds of EEG and behavioral arousal on stimulating the mid-brain reticular formation in unanesthetized unrestrained female rabbits with chronically implanted electrodes. In ovariectomized estrogen-primed animals the subcutaneous injection of 2 mg progesterone was followed within 2-4 hr by a marked reduction of the arousal threshold (down to as low as 10-30% of the pre-progesterone level). During this phase vaginal stimulation with a glass rod induced a sleep-like after-reaction which could be duplicated by low frequency, low voltage electrical stimulation of the ventromedial region of the hypothalamus. The arousal threshold rose again after 6-8 hr and by 24 hr after progesterone it had reached a level of 300-600% of the pre-progesterone threshold. At this stage the rabbit would not mate even with an aggressive buck, and the after-reaction to artificial stimulation of the vagina was absent. The thresholds for evoking sleep spindles on hypothalamic stimulation closely paralleled the arousal thresholds on stimulation of the reticular formation.

EFFECTS OF CARRIER UPON DISTRIBUTION OF CALCIUM-45 AND STRONTIUM-89 IN RATS. Bergene Kawin (intr. by D. H. Copp). Biology Operation, Hanford Labs., General Electric Co., Richland, Washington.

Intraperitoneal and intragastric administration of stable calcium or strontium in amounts up to 3000 μg/gm body weight did not decrease the fraction of simultaneously administered Ca-45 or Sr-89 deposited in tissues of 565 rats. Under certain conditions the data showed significant positive dependencies of radiocalcium and radiostrontium tissue retention on stable calcium or strontium administration. Dependency was, in general, positive in bone if the radioactive metals were fed, and positive in soft tissues following intraperitoneal injection. The data suggested that positive dependence was greater for radiocalcium than for radiostrontium. (Based on work performed for the Atomic Energy Commission under Contract W-31-109-Eng-52.)

CORTICAL AND PERIPHERAL RESPONSES TO VIBRATORY STIMULATION OF THE CAT'S VIBRISSAE. W. D. Keidel, U. Keidel and N. Y-S Kiang (intr. by S. S. Stevens). Research Lab. of Electronics, Massachusetts Inst. of Technology, Boston.

Gross electrodes were placed on the maxillary nerve and the somatic areas (I and II) of the cat's cortex (Dial anesthesia). Evoked responses to mechanical stimulation of the vibrissae were recorded; these mechanical stimuli were obtained by driving an electromechanical transducer by electrical pulses. Trains of pulses were delivered at various intensities and repetition rates. Responses from both cortex and periphery were examined for their behavior in the steady state and in the initial transition period. Both peripheral and cortical responses vary with repetition rate; however, the first few responses in each train are systematically larger than the steady state responses. From these data, amplitude-versus-intensity functions are plotted for both peripheral and cortical responses. These functions are clearly steeper for the transition interval responses than for the steady state responses. The time course of adaptation can be assessed from the way in which response amplitudes change within a train of stimuli. This time course is significantly different at the cortex from that at the periphery. A similar difference is found for cortical and peripheral responses in the auditory system. (Supported in part by the U. S. Army, U. S. Air Force, and U. S. Navy.)

OFF-RESPONSES FROM THE CAT'S AUDITORY CORTEX. N. Y-S Kiang and T. T. Sandel (intr. by S. S. Stevens). Research Lab. of Electronics, Massachusetts Inst. of Technology, Boston.

Off-responses to bursts of tone at the auditory cortex of cats under barbiturate anesthesia are elicited only when there is a marked change in the spectral composition of the acoustic stimulus as it is turned off. We conclude that these so-called off-responses are, in fact, responses to new sets of spectral components that fire neural elements that have been inactive during the period that precedes the off transient. In unanesthetized cats with high spinal sections, however, we have found off-responses that seem not to be produced by additional components in the acoustic spectrum. These off-responses differ from those seen in anesthetized cats in several important ways: 1) They are observed when bursts of noise are turned off and can be completely abolished by injections of barbiturate; 2) their latency is from 6-8 msec longer than the latency of the spectrally induced off-responses; 3) they are less sensitive to changes in stimulus parameters such as duration and fall time. We suggest that we are dealing with genuine off-responses involving neurons other than those which generate on-responses, neurons possibly involving inhibitory links at some intermediate level. (Supported in part by U. S. Army, U. S. Air Force and O.N.R.)

PULMONARY CAPILLARY BLOOD FLOW PULSE IN PATIENTS WITH ALTERED PULMONARY CIRCULATORY DYNAMICS. P. Kimmel*, M. Stein* and A. B. DuBois. Dept. of Physiology and Pharmacology, Grad. School of Medicine, Univ. of Pennsylvania, Philadelphia.

The finding of pulsatile pulmonary capillary blood flow in normal subjects (Lee and DuBois, J. Clin. Invest. 34:230, 1955) led to the study of patients with pulmonic or mitral valve disease or pulmonary vascular disease. All patients had cardiac catheterization within 48 hr prior to this study. The patient sat in a body plethysmograph and inspired a single breath of 80% N_2O, 20% O_2. The internal pressure of the plethysmograph was recorded simultaneously with the patient's ECG. The pulsatile pressure drop due to uptake of N_2O in the pulmonary capillaries was converted to instantaneous blood flow ($\dot{Q}_c$). In some of the patients, as in normal subjects, the notches and peaks of the flow pulse resemble the contour of the pulmonary capillary pressure gradient but lag by approximately 0.1 sec. In others with marked pulmonary hypertension due to pulmonary vascular disease, the $\dot{Q}_c$ wave is markedly distorted and lacks the characteristic presystolic notch and systolic flow peak. In pulmonic stenosis the systolic peak of flow is prolonged. In 3 cases of mitral insufficiency an accentuated secondary

peak of flow is observed in diastole. It is apparent that the measured vascular pressure gradient across the pulmonary capillaries is not the true pressure gradient at the point of N_2O uptake in some patients with pulmonary hypertension. In these cases Q_c was low at some points in the cardiac cycle in the presence of an appreciable pressure gradient.

OLFACTORY RESPONSE OF FROG. Katsumi Kimura (intr. by L. M. Beidler). Div. of Physiology, Florida State Univ., Tallahassee.

The response of the primary olfactory nerve has been reported by Beidler and Tucker (Science 122:76, 1955), and the change in the sustained potential of the olfactory tissue with odor has been revealed by Ottoson (Acta Physiol. Scand. 35, Suppl. 122, 1956). Hartman has described similar sustained potential changes in response to odor in non-biological system (Proc. Am. Soc. Hort. 56:315, 1954). The present investigation correlates the response recorded directly from the primary olfactory nerve of the frog with the change in the sustained potential of the olfactory tissue in response to an odor passed over the olfactory area. Nerve activity and the sustained potential both increase with increase of odor concentration applied to the surface of the nasal cavity. In general the nerve activity parallels that of the sustained potential. Both activities are reduced by repeated stimulation, particularly at high odor concentrations. When Ringer's solution is applied to the olfactory tissue both types of activity are reduced, but soon recover. Cocain or ether cause diminution of both activities but the sustained potential recovers at a time when the nerve discharge has not yet been restored. (Supported partially by a grant from Natl. Science Fndn.)

L-THYROXINE AND L-TRIIODOTHYRONINE EFFECTS ON TISSUE METABOLISM. H. M. Klitgaard and R. A. Whaley*. Dept. of Physiology, Marquette Univ. School of Medicine, Milwaukee, Wis.

Time-response curves for the oxygen consumption of rat tissues to single equmolar injections of L-thyroxine and L-triiodothyronine were determined. The oxygen consumption of kidney, liver, heart, gastric mucosa, skeletal muscle, diaphragm and smooth muscle was followed over a period of 9 days after the injection of the respective hormone. The Q_{O2}'s of all tissues except smooth muscle were significantly increased over the control values. The earliest response to either hormone occurred 12 hr after injection in liver, kidney and cardiac muscle; all reactive tissues had elevated Q_{O2}'s within 24 hr and reached their maximal values in three days with the exception of skeletal muscle. In the latter instance there was a continuous rise for at least 9 days. The maximum Q_{O2} reached on the 3rd day was independent of the injected material; however the rate of decline in oxygen consumption differed significantly. All tissues from thyroxine injected animals maintained a near maximum Q_{O2} through the 9th day except for cardiac muscle; all the tissues from triiodothyronine injected animals (except skeletal muscle) showed significant decreases by the 7th day.

EVIDENCE OF CENTRAL NERVOUS SYSTEM INFLUENCE UPON THE COLD-INDUCED ACCELERATION OF THYROIDAL I^{131} RELEASE IN THE HAMSTER. Karl M. Knigge (intr. by Carmine D. Clemente). Univ. of California at Los Angeles, School of Medicine, Dept. of Anatomy and VA Hosp., Sepulveda.

During the initial 12 hr of cold exposure (5°C) of the hamster, thyroidal I^{131} release is accelerated markedly. Bilateral nephrectomy, adrenal demedullation or adrenalectomy do not influence this response. Appropriate bilateral median eminence lesions placed 24 hr before cold exposure do not interfere with subsequent normal thyroidal release but do block the accelerated release attendant upon cold exposure. Hypophysectomized hamsters exhibit a mean I^{131} uptake of 0.71% compared to a control value of 3.86%. Hypophysectomized animals treated daily for 5 days with 0.01 and 0.05 u of TSH have 12-hr uptakes of 4.80 and 16.2% respectively. After this uptake is achieved and exogenous TSH discontinued, release from the thyroid is slow and cannot be accelerated by cold. In 11 of 14

hypophysectomized hamsters, auto-transplantation of 1 or 2 pituitary glands into the cheek pouch significantly increases I^{131} uptake from a mean control value of 0.64% to 2.03% when tested 5-15 days later. Thyroidal I^{131} release in animals with cheek pouch grafts is not accelerated by cold exposure. These experiments indicate that the cold-induced acceleration of thyroidal I^{131} release, depending upon increased secretion of TSH, requires the pituitary gland with its normal anatomical connections to the central nervous system.

DENSITY, WATER, FAT AND NITROGEN IN HUMAN ADIPOSE TISSUE REMOVED IN SURGICAL OPERATIONS. H. J. Krzywicki*, C. F. Stewart*, J. E. Roberts* and T. H. Allen. U.S. Army Med. Nutrition Lab., Denver, Col.

The density of approximately 1 gm pieces of adipose tissue (omental, perirenal, inguinal and subcutaneous) was determined at 26°C by weighing on a hook in air and then in kerosene. Water was determined by drying at low pressure and at 55°C. Fat was determined by extraction with ethyl ether. Results for 256 tissues show the densities and water contents to commence at 0.91 gm/ml and 5% water and to rise to 0.96 gm/ml at 28% water. Generally, the adipose tissue from obese patients was low in density and water content as compared with the tissue from thin patients. The density of the extractable fat in 121 tissues was computed to be 0.903 gm/ml. Although the percentage of fat in the fresh tissues ranged from 60 to 92, the water content of the fat-free tissue was remarkably close to 79.5%. The nitrogen was approximately 0.035 gm N/gm fat-free tissue, being indicative of a high collagen content. This method gives information as to the water content and density of fat-free muscle, brain, liver, intestines, tendon etc. Accordingly, a mathematical system without any sizeable constant error will be discussed for the computation of the mass of fat in humans, provided that bone mineral of density 2.8 and zero water content is removed from the observed body water and density results.

UNUSUAL FORM OF "MYOTONIA. Edward H. Lambert and Norman P. Goldstein*. Mayo Fndn., Rochester, Minn.

In the course of study of patients with myotonia congenita a person with a different and unusual abnormality of relaxation of muscle was discovered. After a strong voluntary contraction, muscles relaxed slowly over a period of 10 sec in contrast to less than 1 sec in normal persons. With repeated contractions stiffness tended to become more marked rather than to disappear as is the case in myotonia. Quinine and procaine amide had no significant effect. Slowness of relaxation was not due to repetitive activity of muscle fibers as it is in the usual forms of myotonia. Insertion of a needle electrode into the muscle failed to detect any abnormal irritability of muscle fibers. Normal motor unit potentials, observed during voluntary contraction, were under perfect voluntary control and ceased to occur immediately with the patient's intent to relax, although mechanical relaxation was delayed. No electric activity occurred during the prolonged period of relaxation in contrast to the occurrence of repetitive action potentials during the prolonged period of relaxation in recognized forms of myotonia. Both the contraction and relaxation phases of the twitch of the adductor pollicis muscle evoked by a maximal stimulus to the ulnar nerve were prolonged (about 50%) with no abnormality of the associated action potential. This is similar to the slowing of the twitch in myxedema, but no other features suggested abnormality of this type. The abnormality of the contractile system in this person (age 28) was congenital and is said to be present in two brothers but not in other members of the family (including twin sister and another sister and brother).

VAGAL GASTRIC SECRETORY NERVES IN THE RAT DEMONSTRATED WITH INSULIN. Ardelle Lane*, A. C. Ivy and E. K. Ivy*. Dept. of Clin. Science, Univ. of Illinois, and Dept. of Physiology, Dental School, Northwestern Univ., Chicago.

It was found in 4 tests on each of 12 rats with a chronic gastric fistula and accustomed to the experimental procedures, that insulin hypoglycemia short of

convulsions stimulated gastric secretion when the vagus nerves were intact. In 5 tests on each of 7 rats, it was found that section of the vagi abolished the secretory response to insulin hypoglycemia. This evidence is interpreted as establishing the presence of gastric secretory nerves in the vagi of the rat.

ADRENAL, HYPOPHYSEAL, AND PANCREATIC RESPONSE TO STRESS. L. L. Langley and C. H. Gunthorpe*. Dept. of Physiology, Med. College of Alabama, and Univ. of Alabama School of Dentistry, Birmingham.

It is well established that the livers of fasting rats exposed to the stress of low atmospheric pressure accumulate glycogen markedly. It has also been amply confirmed that this glycogen deposition requires the presence of adrenocortical hormone, but this hormone is not solely responsible for the accumulation. The administration of 3 cc of adrenocortical extract (Upjohn) to an adrenalectomized rat fasted at sea-level fails to cause liver glycogen deposition. Such animals under low atmospheric pressure, however, accumulate about 1% liver glycogen. Adrenalectomized-hypophysectomized rats maintained on a minimal dose of hypophyseal extract, given 3 cc of adrenocortical extract and stressed do not deposit liver glycogen. These results suggest that the hypophyseal hormones function not only to control the adrenal cortices under these conditions, but also may contribute directly to the observed carbohydrate alterations. When larger doses of hypophyseal hormones are used there is a significant difference in liver glycogen between the stressed and non-stressed groups indicating the possible implication of still another substance. Since alloxan diabetic rats do not accumulate liver glycogen in response to low atmospheric pressure it is concluded that insulin may also play a key role.

EFFECT OF EPINEPHRINE ON THE RATE OF URINE FORMATION. Jimmy B. Langston* and Arthur C. Guyton. Dept. of Physiology and Biophysics, Univ. Med. Ctr., Jackson, Miss.

The effects of epinephrine administration on urine output have been studied, first, with arterial pressure controlled at constant levels and, second, with arterial pressure allowed to vary with the administration of epinephrine. In both cases complete spinal anesthesia was maintained by intrathecal injection of metycaine hydrochloride. When no attempt was made to control arterial pressure the rate of urine formation increased with each increase in epinephrine administration. This increase in urine flow reached a peak when 0.0008 mg/kg/-min of epinephrine were given intravenously. With further increase in the rate of epinephrine infusion, the urine flow decreased until complete anuria resulted. When arterial pressure was controlled at approximately 70 mm Hg, epinephrine infusion at increasing rates resulted in progressive decrease in urine formation. Similar results were obtained when arterial pressure was maintained at approximately 107 mm Hg except that more urine was formed at each dosage level of epinephrine until anuria resulted. It is concluded that epinephrine affects urine formation in 2 ways: first, by increasing the arterial pressure which in turn increases urinary output and, second, by a direct effect on the kidney to decrease the output. This dual mechanism explains the increased urinary output which usually follows administration of small amounts of epinephrine, and it also explains the anuria that results from massive doses of epinephrine. (Aided by grant from the Natl. Heart Inst. USPHS.)

BIOELECTRIC ACTIVITY OF THE HUMAN UTERUS IN LABOR: SOME PHYSICAL BASES. S. D. Larks (intr. by W. A. Selle). Depts. of Biophysics and Obstetrics and Gynecology, School of Medicine, Univ. of California, Los Angeles.

By means of simultaneous recording from the right and left sides of the uterus in active developing labor, typically repetitive patterns are shown for each side. The left side waveform shows an initial large spike-like variation, followed by a sharp diphasic reversal and thereafter slow recovery. On the right side, activity seems to begin earlier, consisting of an oscillatory discharge during the contractile epoch, followed also by diphasic reversal and slow

recovery. It is shown that the equations and waveform derived by Wilson for the case of radial excitation from a single source show a strong resemblance to the observed left-sided uterine electric waveform. The cited equations were calculated on the assumption that the wave of excitation was accompanied by sources and sinks, i.e. upon dipole considerations. From this agreement between mathematical prediction and experimental observation, it seems reasonable to suggest that the human uterus in labor behaves functionally as a single chambered organ in which excitation spreads radially from a single dominant source. It would seem that the source is relatively distant from the left side. A consideration of the waveform as observed on the right side suggests that the oscillatory pattern is related to pacemaker activity. This concept is supported by parallel investigation at the cardiac SA node which demonstrates specific pacemaker electric activity. It is therefore considered probable that: 1) the human uterus behaves functionally as a single chambered organ; 2) excitation generally arises in a single dominant pacemaker under normal conditions; 3) the wave of excitation spreads radially; and 4) present information suggests that the pacemaker is generally on the right side. (Supported by grant-in-aid from the USPHS, RG-4462.)

EFFECT OF PARTIAL UNILATERAL RESECTION ON BILATERAL STATIC COMPLIANCE, FUNCTIONAL RESIDUAL VOLUME AND TIDAL VENTILATION. M. T. Lategola and J. A. Schilling (intr. by A. N. Taylor). Depts. of Physiology and Surgery, Univ. of Oklahoma Med. School, Oklahoma City.

Following suitable control determinations, the medical, lower and mediastinal lobes (lobes BCM) of the right lung were removed in the 1st group of 4 dogs and the upper and medial lobes (lobes DE) of the left lung were removed in the 2nd group of 4 dogs. All surgery was performed under standard aseptic conditions. Based on the relative lobe weights as reported by Rahn et al. (J. Appl. Physiol. 8:417, 1956), 41.1% of the whole lung was removed in the 1st group of dogs and 15.4% in the 2nd. Experimental measurements were made on the Nembutalized, supine dogs post-operatively on the 10th, 40th and 80th days. In both groups the static compliance of the operated hemi-chest was markedly reduced. Relative to predicted values, the remaining right upper lung segment of the 1st group was overventilated whereas the left lower lung segment of the 2nd group was underventilated. In correlation with these latter observations, the functional residual volume of the right upper segment of the 1st group has increased over predicted values whereas the left lower segment of the 2nd group has decreased. (Supported by funds from the School of Aviation Medicine, Randolph Field, Texas; AF contract #41(657)-105.)

CHANGES IN SPECIFIC GRAVITY IN THE MALE ALBINO RAT WITH AGE. J. Laverty* and E. DaCosta. Chicago Teachers College, Chicago, Ill.

The specific gravity of 99 albino rats between the ages of 7 and 116 wk, and fed mainly Purina Laboratory Chow ad libitum, was determined by underwater weighings. Separate data were secured on, 1) tail-less, shaved rats, 2) viscera, 3) eviscerated, tail-less, shaved rats, 4) skin, and 5) skinned, eviscerated, tail-less rats. The greatest changes were found in the skinned, eviscerated group. Thus the specific gravity in the 7-wk group was 0.9734, and rose to 1.0709 in the 20-wk rats. Between 20 and 44 wk the specific gravity averaged at 1.0588, and was 1.0715 at the 44-wk level. The specific gravity rapidly declined after this to 1.0164 in the 60-wk-old group, and the lowest, or 0.97992, in the 114-wk group, although the 115- and 116-wk groups had specific gravities of 0.99567 and 0.99790 respectively. Least change was found in the specific gravity of the viscera. The general results indicated that the specific gravity increased until the rats were about 20 wk old, remained relatively stable until they were 44 wk old, and then declined. Thus the period in which lean body mass was greatest, and the fat least, was evidently between 20 and 44 wk of age.

MAST CELL CHANGES IN ANIMALS EXPOSED TO COLD. J. LeBlanc and F. Rosenberg (intr. by F. N. Craig). Applied Physiology Branch, Directorate of Med. Research Army Chem. Ctr., Md.

The frequency of occurrence of mast cells of different tissues of rats was investigated at 2° and 6°C. In the mesentery the number of these cells increased in the perivascular region after exposing the animals for 2 and 4 wk at 6°C; in the intervascular region the number decreased after 2 wk but returned to the initial value after 4 wk. The same changes were observed in animals exposed at 2°C. In the skin of the abdomen an increase was observed at both temperatures after 2 wk. In the skin of the ear, which is much more exposed to the environmental temperature than the abdomen, a significant drop was observed after 2- and 4-wk exposures to 2 and 6°C. However, the decrease was significantly larger at 2°C than at 6°C. The increases in number of mast cells in abdominal skin and the changes in the mesentery are considered to be systemic effects of cold; the decreases in the skin of the ear are considered to be local effects.

NEUROMUSCULAR TRANSMISSION IN COLD TEMPERATURE. Choh-luh Li and Peter Gouras*. Natl. Inst. of Neurological Diseases and Blindness, Bethesda, Md.

Recording with intracellular microelectrodes from neuromuscular junctions of isolated sartorius muscle of frogs revealed that transmission of impulses took place at temperature as low as -1°C. The resting membrane potentials were found to be virtually unchanged at temperature between 25°C and -1°C. During the process of cooling the spontaneous minature endplate potentials showed a decrease in frequency and an increase in amplitude, but at about 5°C the amplitude began to drop while the frequency continued to be low. Also at about 5°C and below stimulation of the motor nerve frequently failed to evoke a spike discharge and at -1°C a complete blockage of the neuromuscular junction was observed. It is postulated that there is a critical temperature for neuromuscular transmission at about 4 or 5°C, below which an appreciable resistance is encountered before a complete blockage takes place. This investigation also suggests that contracture activity of skeletal muscle fibers could be brought out by cooling.

EFFECTS OF HEART RATE ON ATRIO-VENTRICULAR CONDUCTION. Juhan Liikane*, Allen M. Scher, Malcolm Fishback* and Leland Burnett*. Dept. of Physiology and Biophysics, Univ. of Washington School of Medicine, Seattle.

Previous experimental studies of A-V conduction have utilized recordings from atrial and ventricular points alone. The use of various stimulation frequencies has established that with increased frequency of stimulation, the overall A-V conduction time increases. This increase has generally been attributed to alterations of conduction in the A-V node. In our studies we have analyzed continuous, moving-film recordings from a multichannel oscilloscope and intramural multipolar electrodes. Intramural electrodes were placed in atrial muscle near the A-V node, in the common bundle, and also in the atrial and ventricular muscle. Our stimulator was set at a basic frequency of stimulation and the last pulse of each stimulus train was independently variable. The results indicate that previously noted effects of the heart rate on the A-V conduction time cannot be attributed to the A-V node alone. Atrial muscle near the A-V node and the conduction pathways downstream from the node also show different conduction velocities with alterations in the heart rate. In the order of decreasing susceptibility to changes in stimulation frequency are ranked 1) the A-V node, 2) the atrial muscle and 3) the Purkinje conducting structures. (Aided by Grant H-1315, from the USPHS and by a grant from the American Heart Assoc.)

CONTINUOUS RECORDING OF PULMONARY BLOOD VOLUME IN THE INTACT ANIMAL. Arthur W. Lindsey* and Arthur C. Guyton. Dept. of Physiology and Biophysics, Univ. of Mississippi Med. Ctr., Jackson.

By using a gamma emitting plasma or red cell tag plus proper collimation of a radiation detector it has been possible to record continuously the amount of radiation from a circumscribed area of the lung field. After subtracting the

background radiation from the chest wall, the remainder of the detected radiation has been found to vary proportionately with changes in pulmonary blood volume. Calibration of the system is performed at the end of the experiment by injecting known quantities of radioactive blood into the pulmonary circulation. During the experimental procedure the pulmonary artery or aorta is constricted by previously placed plastic loops that can be manipulated by pulling a tube protruding from the animal's back. Following pulmonary artery constriction the pulmonary blood volume decreases more than 50% in some animals, and the pulmonary artery pressure decreases to a negative value. When the ascending aorta is constricted the pulmonary blood volume increases more than 100%, and the pulmonary artery pressure increases up to 60-70 mm Hg in some animals. Using this continuous recording system is has been observed that the pulmonary blood volume, in general, changes proportionately with pulmonary artery pressure when acute heart failure is induced. (Supported by a grant from the Life Insurance Med. Research Fund.)

AROMATIC ESTERASE IN HUMAN SERUM. H. A. Lindsay (intr. by E. J. Van Liere). West Virginia Univ., Morgantown.

An optical method for the determination of aromatic esterase activity has been developed. Application of this method to a rather small group of subjects showed an arithmetical, but not statistical, difference between the means of esterase activity in male and female subjects (Lindsay, Ph.D. thesis, Univ. of Toronto, 1955). Study of a larger group of subjects failed to increase the probability of a sex difference in aromatic esterase activity but provided a better estimate of the variation between subjects. The variation within subjects from day to day has also been determined. Values for the Michaelis constant and temperature coefficient of the aromatic esterase-phenyl acetate system have been determined.

TRYPTOPHAN INHIBITION OF THE IN VITRO EFFECT OF THYROXINE ON OXYGEN CONSUMPTION OF RAT KIDNEY SLICES. R. H. Lindsay* and S. B. Barker. Dept. of Pharmacology, Univ. of Alabama Med. Ctr., Birmingham.

Recent work in this laboratory demonstrated an effect of thyroxine which resulted in a higher rate of oxygen consumption of rat kidney slices incubated at 5°C between measurements of oxygen uptake at 37°C. The thyroxine effect was apparent with endogenous substrates and became more pronounced in a Ringer-DL-alanine-glucose medium. Tissue in this medium maintained approximately 80% of the initial Q_{O_2} after 3 days of incubation in the presence of thyroxine compared to 15% for the tissue without thyroxine. A survey of the effects of 50 amino acids and related compounds showed that only DL-alanine, L-proline, DL-asparagine and N-acetyl-DL-alanine were outstanding in their ability to enhance the effect of thyroxine. The better maintenance of oxygen uptake in the presence of thyroxine was apparent with all the compounds tested except L-tryptophan. This amino acid depressed the Q_{O_2} when present in Ringer, Ringer-glucose and Ringer-alanine-glucose media, especially Ringer-alanine-glucose which usually produced a high rate of oxygen consumption. L-Trytophan blocked completely the action of thyroxine in Ringer and Ringer-glucose media resulting in no difference in maintenance between tissue in the presence or absence of thyroxine. It not only blocked the effect of thyroxine in Ringer-alanine-glucose, but after 24 hr of incubation the tissue with added thyroxine consumed oxygen at a lower rate than the controls. (Supported by grants from the American Cancer Soc. and the Smith, Kline and French Fndn.)

EFFECT OF ANEMIC RABBIT PLASMA ON Fe^{59} UPTAKE AFTER X-IRRADIATION. W. H. Linkenheimer* and W. C. Grant. Research Div., American Cyanamid Co., Pearl River, N. Y.

It is known that x-irradiation depresses bone marrow function. It is also established that there is a factor in raw or boiled anemic rabbit plasma that will stimulate erythropoiesis in the normal animal. The purpose of this paper is to

present data showing differences in Fe^{59} uptake by the red cells with and without x-irradiation and the influence of anemic rabbit plasma administered after exposure. Rats were exposed to 125 r. Within 1 hr after the exposure the animals were injected with anemic rabbit plasma, normal rabbit plasma, or saline, S.C. Fe^{59} was injected 24 hr later by vein. Blood samples were obtained 18 hr after Fe^{59} injection. Control animals were treated similarly, but not exposed to x-irradiation. When unexposed rats were injected with raw or boiled normal rabbit plasma, Fe^{59} uptakes of 65 and 63% respectively of injected dose were noted. X-irradiated animals receiving the same materials had only 27 and 25%. Raw or boiled anemic plasma given to unexposed rats produced Fe^{59} uptakes of 84 and 79%. When this plasma obtained from anemic animals was given to irradiated rats uptakes of 56 for raw and 41% for boiled were obtained. The data suggest that raw or boiled anemic rabbit plasma will stimulate erythropoiesis either before or after x-irradiation. However, boiling appears to destroy more activity when plasma is tested after x-irradiation.

INHIBITION OF IODIDE TRAP ACTIVITY IN THE GOITROUS MOUSE THYROID. H. J. Lipner, Billie P. Wagner and H. P. Morris (intr. by Dexter M. Easton). Div. of Physiology, Florida State Univ., Tallahassee, and Lab. of Biochemistry, Natl. Cancer Inst., Bethesda, Md.

There are 2 methods for expressing the iodide trapping activity of the thyroid gland. The first is a measure of the specific activity of the thyroid iodide trap: T/S = I^{131}/100 mg thyroid: I^{131}/0.1 ml serum (Vanderlaan, W. P. and Greer, M. A. Endocrinology 47: 34-47, 1950). The second is a measure of total iodide trap activity of the thyroid gland: t/S = I^{131}/total thyroid weight: I^{131}/0.1 ml serum (Halmi, N. S. Ciba Fndn. Colloquia on Endocrinology 10: 79-94, 1957). Both methods were applied to the following experiments. Diets containing propylthiouracil (PTU) in concentrations of 0.00078% to 0.025% were fed to mice for 28 days. As the dose of PTU was raised, the thyroid weight increased, while the T/S decreased. The latter was inversely proportional to the thyroid weight. The t/S increased directly with the gland weight. This experiment may be interpreted as either evidence of "dilution of iodide acceptor sites" (Halmi, ibid.) or of blockade of these sites. Halmi has suggested that thyrotrophin (TSH) is the material that is responsible for the blockade. We think the following experiment is further confirmation of this concept. Mice were fed a diet containing 0.025% PTU for 30 days and then returned to the basal diet. The T/S was determined on the same day the basal diet was restored and subsequently at daily intervals for 4 days and again on the 8th day. Both the T/S and the t/S reached a peak on the day after the return to basal diet. PTU results in depletion of iodine from the thyroid. At the time the peak T/S is reached the TSH level is probably declining. It is therefore probable that the depression in the activity seen in the thyroid iodide trap is a function of the concentration of TSH in the gland. (Supported by a fellowship from the National Cancer Inst. USPHS.)

INHIBITION BY LUNG STRETCH OF ACTIVITY IN THE RECURRENT LARYNGEAL NERVE AND THE TRACHEAL MUSCLE. G. N. Loofbourrow and William B. Wood*. Dept. of Physiology, Univ. of Kansas, Lawrence.

In eupnea, action potentials in phase with inspiration are found in afferent vagal fibers from lung stretch receptors. Similar phasic patterns are found in efferent fibers of the recurrent laryngeal nerve, leading to phasic contractions of laryngeal muscles. All these phasic activities are increased during hyperpnea induced by hypercapnia or asphyxia. During this period of increased phasic activity there is also a striking, slow, apparently non-phasic contraction of the tracheal muscle. Strong, sustained inflation of the lungs provides strong, sustained afferent activity of lung stretch receptors and their afferent vagal fibers. During this activity, both the phasic responses and the tonic contraction of the tracheal muscle are abolished or markedly diminished.

HYPERTROPHY AND CHANGES IN CHOLINESTERASE ACTIVITIES OF INTESTINE, ERYTHROCYTES AND PLASMA, FOLLOWING "MINIMAL"

RESECTION OF THE SMALL INTESTINE OF THE RAT. M. R. Loran and T. L. Althausen (intr. by Leslie L. Bennett). Gastrointestinal Research Lab., Dept. of Medicine, Univ. of California School of Medicine, San Francisco.

Previous work demonstrated that 10% resection of the small intestine of the rat resulted in a lasting nearly 50% decrease in vitamin A absorption. Histological examination showed considerable hypertrophy of the resected intestine (Gastroenterology 31:717, 1956). Data are presented to quantitate this hypertrophy and to explore certain changes in the cholinesterase activities of the intestine and blood. Six weeks following 10% resection of the upper jejunum, the small intestine was found to be 21% shorter than normal. However, the wet weight of the remaining 90% of the intestine was restored to the weight of the intact intestine, indicating a 13% increase in the weight of the remaining portion. The dry weight of the resected intestine was 13% greater than the dry weight of the controls, amounting to a 26% increase in the solids of the remaining portion. Cholinesterase activities were determined against 3 substrates (ACH, BCH and MCH). Six weeks following resection the total cholinesterase activity (ACh) of the intestine was identical with the controls. However, activity toward BCh was significantly greater for the resected intestine than for the controls. There was also a marked increase in the activity toward BCh in the plasma of the resected animals. Studies on the cholinesterase activity of the erythrocytes showed an increase in total esterase activity (ACH) and in specific esterase activity (MCh) in the resected animals. Control studies after "sham" operations and after simple transection of the small intestine indicate that the intestinal hypertrophy and increase in cholinesterase activities following "minimal" resection is due to removal of intestinal tissue rather than the abdominal operation per se.

EFFECTS OF SUCCESSIVE DOSES OF L-EPINEPHRINE ON CIRCULATORY DYNAMICS. Peter R. Lynch* and M. J. Oppenheimer. Dept. of Physiology, Temple Univ. Med. School, Philadelphia, Pa.

Dogs anesthetized with sodium pentobarbitol were given 3 successive doses of l-epinephrine; 1) 100th, 2) 1, and 3) 1 mg/kg. The first dose served as a means to protect the heart against ventricular fibrillation and asystole which frequently follow massive doses of epinephrine (Essex, H. E., Am. J. Physiol., 171:1952). The second injection (10 min after the first) of l-epinephrine caused marked alterations in the electrocardiogram, blood pressure and respiration. The 3rd injection (between 10 and 30 min after the 2nd) however, frequently was followed by much reduced responses. Plasma (5-10 ml) removed from the dog after the blood pressure had returned to the control level injected into another dog produced a substantial increase in blood pressure. This could be interpreted as evidence that l-epinephrine can remain in the circulation in an active state without demonstrating its activity in animals given massive doses of the drug. The bearing of this finding on the increased tolerance to successive large doses of l-epinephrine is being investigated.

MEASUREMENT OF VALVULAR INCOMPETENCY IN VARICOSE VEINS. Ian F. S. Mackay. Dept. of Physiology, Univ. College of the West Indies.

Two techniques have been devised to measure the degree of valvular incompetency in varicose veins, (Mackay, I. F. S. and McCarthy, G. S., in press; Mackay, I. F. S. Ciencia 16:79, 1956). The first procedure was to promote venous backflow and measure this plethysmographically. It is done by a tilting procedure with, and then without, a pressure cuff which compresses the veins. It gives an indication of the degree of valvular incompetency in the whole limb. The venous backflow thus recorded in varicose veins is prevented by operative ligation. Time flow-rate curves had to be devised to measure the venous backflow rates. The second technique was devised in order to measure valvular incompetency in a segment of the limb. It consisted of a nylon band which could be applied at known pressures to a limb, causing the displacement of blood from the veins. The rate of the recovery of the displaced volume is measured plethysmographically while the subject is in the upright position. This recovery

rate is much more rapid in subjects with varicose veins than in normal subjects, which is probably due to the return of the blood past the incompetent valves into the area that was previously compressed.

EFFECT ON THE RAT PANCREAS OF ALTERNATING THE AMOUNT OF DIETARY PROTEIN. D. F. Magee. Dept. of Pharmacology, Univ. of Washington, Seattle.

Thirty-two rats were divided into 4 groups, each group comprising 4 males and 4 females. Group 1 was fed a diet containing 6% casein as the sole source of protein. Group 2 received 6% casein for 6 days and 18% for 1 day only. Group 3 received 6% for 3 days and 18% for 2 days. Group 4 received only 18% casein. The protein changes were made at the expense of carbohydrate. In all other particulars the diets were identical. This feeding schedule continued for 4 wk. The animals were then killed and the pancreases removed. Each animal ate 12 gm of food daily. All of the group gained weight. Those on the alternating diets, however, gained less than either control. It was found that group 2 animals had as much proteolytic activity per pancreas as group 4, but since the mean pancreatic weight was as low as group 1, the concentration was much (33%) higher than group 4. The total proteolytic activity and the concentration in group 2 is significantly greater than group 1. The pancreas weights in group 2 are significantly smaller than group 4. Group 3 in all the particulars discussed occupied an intermediate position between groups 1 and 4.

STOP FLOW ANALYSIS OF RENAL TUBULE LOCALIZATION. R. L. Malvin*, L. P. Sullivan* and W. S. Wilde, Dept. of Physiology, Univ. of Michigan, Ann Arbor.

Localization of renal tubular transport of substances along the length of the nephron of a dog is characterized by allowing concentration patterns to develop during stopped tubular flow (ureteral occlusion with stopped filtration). The pattern is caught in serial urine samples collected rapid-fire from a polyethylene ureteral cannula after the brief occulsion is released. Previous administration of an osmotic diuretic mannitol provides a rapid post-occlusion flow such as minimizes downstream reabsorption-secretion influences upon concentration. The pattern of concentration is oriented along the column of fluid moving out of each nephron. Serial urine samples segment this into an ordered array which is best caught on a graph if concentration of each sample is plotted against the accumulated volume of fluid which has appeared since reinstatement of flow. Plots against time show distortion due to variable flow rate. The filtration indicator inulin is injected late after occlusion to reach the filter surface and be ready to signal new entry of filtrate into the urine samples after the occlusion is released. The rising concentration pattern of this inulin delineates the randomizing effect of variable lengths among nephrons. Paraminohippurate (PAH) injected after occlusion signals entry sites for secretion. These appear ahead of inulin. If glycosuria is developed before occlusion such that the glucose reabsorptive transfer maximum is exceeded, the occlusion now allows further time for lowering of glucose concentration along the tubule. The lowered glucose concentration pattern overlaps that of rising PAH. PAH secretion is proximal in the mammal. Very distal fluid is relatively sodium free. Blood flow is unimpaired during 6-min occlusions. (Aid from Am. Heart Assoc.; Life Insurance Med. Research Fund.)

METABOLIC STUDIES ON EPINEPHRINE AND NOREPINEPHRINE. William M. Manger*, Khalil G. Wakim, Jesse L. Bollman and John H. Grindlay. Sections of Medicine, Physiology, Biochemistry and Surgical Research, Mayo Clinic and Mayo Fndn., Rochester, Minn.

The rate of disappearance of epinephrine and norepinephrine from blood was studied by use of a modification of the method of Weil-Malherbe and Bone for the quantitation of plasma pressor amines. In the dog, the concentration of epinephrine-like substance had practically returned to preinjection levels within 4-16 min after intravenous administration of 10 μg of epinephrine per kg of body

weight. This occurred in the normal animal, in the animal previously made tolerant to large doses of epinephrine and in animals receiving large doses of thyroxin or tri-iodothyronine over long periods. The findings of prolonged infusion experiments suggested that epinephrine may be partially converted to norepinephrine. During a single infusion of norepinephrine, converstion to epinephrine was not evident. After the infusion of epinephrine or norepinephrine had been terminated, the concentration of these amines in the plasma usually required more than 20 min to return to preinfusion levels. The subsequent decrease in plasma concentration of the infused pressor amine was accompanied by a transient increase in the other amine. Comparison of the concentrations of epinephrine-like substance in the plasma, before and after passage of the substance through the liver, revealed that a considerable proportion of the pressor amines was removed or inactivated by the liver. The infusion of marsilid or ephedrine did not appreciably alter the disappearance rate from plasma of either endogenous pressor amines or of exogenous pressor amines administered in a single dose or infused over a long period. The much slower decrease in concentration of epinephrine added to plasma in vitro was minimized by the presence of sodium thiosulfate, but was not affected by ephedrine or marsilid.

QUALITATIVE EFFECT OF PENTOBARBITAL ON THE CIRCULATING HEMOGLOBIN OF THE DOG. Santos Martinez (intr. by Roger M. Reinecke). Dept. of Physiology, Univ. of Puerto Rico School of Medicine, San Juan.

Samples were drawn from the femoral artery and jugular vein before and after pentobarbital anesthesia in the dog. Duplicate subsamples taken from each of these samples were analyzed for hemoglobin by a modification of the Palmer method and by a modification of the Cohen and Smith method (J. Biol. Chem., 33:119, 1918; J. Biol. Chem. 39:469, 1919). An analysis of variance of the results for both the arterial and venous samples taken after anesthesia revealed a statistically significant variation between the results obtained by the 2 methods after anesthesia that could not be accounted for by the variation between the replicate determinations by either of these methods or by the variation between the results obtained by the 2 methods before anesthesia. From this it appears that pentobarbital anesthesia in the dog in some way alters the relative concentrations of the circulating substances measured as carbonmonoxide hemoglobin and as acid hematin.

FIBRILLATION IN DYSTROPHIC MUSCLES. A. R. McIntyre, A. L. Bennett and J. S. Hinman*. Dept. of Physiology and Pharmacology, Univ. of Nebraska College of Medicine, Omaha.

The availability of the Bar Harbor strain of dystrophic mice afforded an opportunity of measuring the resting potential of dystrophic muscles in vivo by the use of the technique previously developed by us for such measurements in normal mice. It had previously been established that the mean resting potential of normal mouse skeletal muscles with intact circulation at normal temperature is 100 m volts, and in mice following denervation, the mean resting potential was 80 m volts. The mean resting potential of dystrophic mouse muscles in vivo was found to be 85 m volts. Histological examination revealed small degenerative areas in the muscles strikingly similar to those seen following denervation. Spontaneous activity identical with the fibrillation of denervation was frequently recorded in the dystrophic mouse muscles. Subsequently fibrillation was recorded from the flexor carpi ulnaris muscles in a case of human myotonic dystrophy. Electromyography from normal, denervated and dystrophic mucles in man and the mouse will be presented and discussed. It is concluded that in some forms of dystrophy spontaneous action potentials of short duration (0.8-1.8 msec) and low voltage 10-100 μvolts (as recorded from a concentric needle electrode) and low rates of repetition (0.5-13/sec) are frequently present. This spontaneous activity is strikingly similar to that seen following denervation.

EFFECT OF HYPNOTIC SUGGESTION ON COLD INDUCED VASODILATATION. John P. Meehan, Jr. and H. I. Jacobs (intr. by Douglas R. Drury). Dept. of Physiology, School of Medicine, Univ. of Southern California, Los Angeles.

A number of studies of the phenomenon of cold vasodilatation have been carried out for the purpose of demonstrating a relationship between the occurrence of the phenomenon in any given individual and his resistance to cold injury. In this connection, physiologic factors that may vary the appearance and extent of cold vasodilatation have been thoroughly investigated. In the experience of the authors, the nature of the phenomenon seen in any given experiment show greater modification when the emotional attitude of the subject is altered. In order to control the factor of emotional attitude, hypnotic suggestions of anaesthesia, lack of discomfort, extreme discomfort and anxiety have been given to subjects whose fingers were immersed in ice water. Finger skin temperatures were recorded potentiometrically from copper-constantan thermocouples cemented to the skin of the fingers. Under controlled conditions, the hypnotic suggestions employed modified the response of any given subject studied to a marked degree. In particular, the onset of rewarming and the shape of the rewarming curve showed the greatest modification. Also, consistent changes in the blood flow of the contralateral fingers were observed. It is our conclusion that the central nervous system can play a significant role in the determination of the occurrence of cold induced vasodilatation and therefore may also play an important role in determining resistance to cold injury.

EFFECTS OF HYPER- AND HYPOTHYROIDISM ON CHEMICALLY-INDUCED SKIN TUMORS IN MICE. Joseph Meites and R. F. Langham*. Dept. of Physiology and Pharmacology, Michigan State Univ., East Lansing.

In 3 separate experiments the effects of feeding thyroxine or thiouracil on skin tumors were studied in mice, painted once over the back with 9,10-dimethyl-1,2 benzanthracene (DMBA) followed by once-weekly applications of a 5% solution of croton oil in liquid paraffin. Approximately 20 female albino mice of uniform age and weight were used per group, and separate controls were employed for each of the 3 experiments. Thyroxine (Smith, Kline and French) and thiouracil were fed in concentrations of 2 mg/kg and 2 gm/kg of diet, respectively, beginning on the same day or 2 wk after application of DMBA. A different dose of the latter was used in each of the 3 experiments, namely 1.0, 0.5 or a 0.25% solution in benzene applied in a volume of .05 ml. In all 3 experiments, thyroxine inhibited while thiouracil increased the total incidence of tumors per group, average number of tumors and average size of tumors. These effects were most marked in the mice which received the smallest dose of DMBA. In general, thyroxine increased while thiouracil decreased food intake and body weight. Histological examination of skin biopsies from these mice indicated that thyroxine accelerated while thiouracil depressed skin and hair growth. The majority of tumors were benign papillomas and a few were carcinomas.

HUMAN MIDDLE EAR MUSCLE RESPONSE TO LOUD SOUNDS. Emanuel S. Mendelson. Naval Air Material Ctr., Air Crew Equipment Lab., Philadelphia, Pa.

In search of a direct effect or correlate of intense acoustic stimulation, the involuntary activity of the intra-aural muscles has attracted recurring attention since the time of Helmholtz and Politzer. We still know little about the normal incidence and nature of tympanic membrane displacements accompanying the auditory reflex despite pioneer efforts during the intervening generations. Kohler's photographic method (1909), recently improved by Kobrak (1957), demonstrates angular displacement of the drumhead in an unspecified fraction of selected subjects. The manometric technique separately applied by Wojatschek (1908) and Mangold (1913) has been tested independently in the present study. Twenty-five laboratory volunteers and 13 volunteer medical students have been used in an attempt to develop a reliable, portable method. Using a sensitive pressure probe in the occluded external meatus, volumetric

displacements up to about 0.5 cu mm have been registered in 10 of the subjects during contralateral airborne stimulation. Effective stimuli corresponded with those classically described as arousing the auditory reflex.

CENTRIFUGAL SEPARATION OF FREE AND BOUND GLYCOGEN. D. K. Meyer. Univ. of Missouri School of Medicine, Columbia.

Dog and rat ventricular tissue, rat skeletal muscle and liver, were homogenized in a Ten Broeck tissue grinder in a medium of 0.32 M sucrose and 0.02 M versene. All procedures were carried at 0°-4°C. The homogenate was separated into myofibril, etc., mitochondria, microsomes and a final supernatant by centrifuging successively at 700 g for 3-1/2 min, 7,500 g for 5 min and 23,000 g for 121 min. Each centrifugal fraction was extracted with cold 10% TCA to separate free glycogen while the residue was digested in KOH to isolate the bound glycogen. Glycogen was determined by the anthrone method. The free and bound glycogen showed similar distributions in heart and in muscle. The final supernatant contained 94-98% of the free glycogen. The coarse particles, separated in the initial centrifugation, contained 62-69% of the bound glycogen compared to 23-34% in the supernatant. Only traces of either glycogen fraction were found in the mitochondria and the microsomes. Liver exhibited a markedly different distribution of free and bound glycogen. The particulate glycogen of Lazarow, which sedimented with the microsomes in an easily separable form, contained 61% of the free and 54% of the bound glycogen. Appreciable quantities of both glycogens were recovered in the microsomes and mitochondria while 10% of the free glycogen and 27% of the bound glycogen was in the largest particles. The final supernatant held 13% of the free and 4% of the bound glycogen. (Supported by a grant from the Dept. of Health, Education and Welfare.)

BLOOD PRESSURE AND THYROID ACTIVITY DURING PROLONGED FASTING AND REALIMENTATION IN NORMAL DOGS. V. W. Meyers*, H. H. McCarthy* and C. M. Wilhelmj. Depts. of Physiology-Pharmacology and Surgery, Creighton Univ. School of Medicine, Omaha, Nebr.

Six dogs were subjected to fasting (28-50 days) followed by realimentation with luxus consumption carbohydrate diets (120 Cal/m^2/hr). Blood pressure studies on 2 of the dogs showed a highly significant fall in systolic and diastolic pressure and pulse rate during fasting. Realimentation with high carbohydrate diets resulted in a significant elevation of systolic pressure and pulse rate with little change in diastolic pressure when compared with controls. Serum protein-bound iodine determinations (178) on the 6 dogs during the experimental periods showed changes that were not considered physiologically significant. On the 4 dogs not used for blood pressure studies, radio-active iodine uptake was determined at the end of each experimental period. The average uptake during the control, fasting and realimentation was respectively 9.2%, 10.6% and 15.6%. The maximal individual changes during fasting were -4.6% and +9%. With realimentation the maximal individual increase in uptake was 8.4%. Following the carbohydrate effect, the 2 blood pressure dogs were given thyroid extract (0.9 gm/-kg/day) for 2 wk. Thyroid produced a cardiovascular response similar to that which occurred with the carbohydrate diet. Protein-bound iodine determinations during the thyroid feeding were above 15 μg/100 cc. Though there were significant changes in blood pressure and pulse rate during fasting and realimentation with high carbohydrate diets, thyroid activity as reflected by protein-bound iodine and radio-active iodine uptake appeared not to be influenced. (Supported by grants from American Heart Assoc. and Natl. Heart Inst., USPHS.)

CHANGE IN BLOOD ASCORBIC ACID OF THE ALBINO RAT WITH AGE. R. C. Mitchell* and E. DaCosta. Chicago Teachers College, Chicago, Ill.

A decline in blood ascorbic acid has been found in man where an exogenous source of vitamin C is needed. The determination of the blood ascorbic acid with rats, which can synthesize vitamin C, was conducted. Eighty-two males and 89 albino females, ranging in age from 4-95 wk and fed Purina Laboratory Chow ad libitum, were used. In the males the blood acorbic acid at 4, 8, 13, 26,

and 95 wk was found to be 2.2, 1.4, 1.9, 1.6, and 1.5 mg% respectively. In the females, the blood ascorbic acid at 4, 9, 15, 26, 51, 72, and 92 wk was found to be 2.2, 1.7, 2.0, 1.7, 1.4, 1.3 to .64 mg% respectively. In short, both sexes showed a decline in blood ascorbic acid which, however, was greater in the females than in the males. The greater decline in the older females may be related to the fact that all had at least 1 litter.

FACTORS AFFECTING THE SEASONAL VARIATION OF GASTRIC HCl PRODUCTION. Sherwin Mizell (intr. by R. E. Johnson). Dept. of Physiology, Univ. of Illinois, Urbana.

Using apparatus modified after Delrue, studies were made in vitro on the effect of temperature and glucose and inosine triphosphate on the production of HCl by the gastric mucosa of Rana pipiens. Throughout all experiments histamine diphosphate was added to stimulate acid production. In the first series of experiments frogs were maintained in a fasted condition for a minimum of 14 days in either a refrigerator at 4°C or at room temperature (25-31°C). Periodic readings of pH were made during the course of acid production, and total acid was measured at the end of each run. A total of 149 frogs (av. 14/month) showed a seasonal variation in acid production which was independent of the temperature at which the animal lived. The cycle showed maximal decreases of pH in late spring and late fall, although all seasons differed significantly from each other. In another series of experiments frogs have been maintained at a constant temperature (21°C) and combinations of 0.10 mM glucose and 0.6 μ M ITP were added as substrates. In 270 animals (av. 30/month) studied from November to August of this year, those receiving either no substrate or ITP alone showed an acid production almost duplicating the previous cycle. However, those animals which received glucose alone or glucose in combination with ITP as substrate maintained a constant acid production which in some months is twice that of the usual cycle.

MYOCARDIAL OXYGEN CONSUMPTION AND CORONARY BLOOD FLOW DURING POTASSIUM-INDUCED CARDIAC ARREST AND VENTRICULAR FIBRILLATION. R. G. Monroe, E. Berglund and G. L. Schreiner (intr. by J. L. Whittenberger). Dept. of Physiology, Harvard School of Public Health, Boston, Mass.

After thoracotomy the left coronary artery of a dog was perfused at a constant pressure from a carotid artery of a donor. Venous blood was returned from the experimental dog to the donor. Aortic perfusion of the experimental dog was maintained during cardiac arrest and fibrillation. Coronary sinus samples were obtained via a catheter. Coronary flow was measured with a Shipley-Wilson rotameter. Myocardial oxygen consumption was determined as the product of coronary a-v difference and left coronary flow. Arrest was induced for an average of 30 min by rapid injection of 10-20 ml of 5% potassium citrate into the left coronary artery followed by a slow infusion of the same solution. Ventricular fibrillation and defibrillation were induced electrically. In 5 dogs, after a steady state had been reached, myocardial oxygen consumption was less than 3 1/2 ml/min. During ventricular fibrillation the oxygen consumption was 4-9 times higher than during arrest. The values during "control" work showed a wide spread due to variations in heart rate and aortic pressure. Immediately following potassium-induced arrest there was a transient increase in coronary flow. Within 5 min a steady state was achieved which showed a lower coronary flow than during the control period. In 4 of the 6 experiments there was a linear relationship between myocardial oxygen consumption and coronary flow. The data suggest that coronary inflow obstruction is less deleterious during arrest than during fibrillation.

THRESHOLD FOR WARMTH DISCRIMINATION IN THE NORMAL AND HYPOTHALECTOMIZED DOG. D. Murgatroyd*, A. D. Keller and J. D. Hardy. Dept. of Physiology, Med. School, Univ. of Pennsylvania, Philadelphia, and Army Med. Research Lab., Fort Knox, Ky.

In a series of calorimeter experiments designed to evaluate the response of normal and dogs with posterior hypothalamic lesions, one preparation was obtained which showed minimal responses to cold and had a definitely elevated panting threshold on exposure to heat. In view of the close relation between temperature sensation and temperature regulation it was decided to measure the threshold response of the normal and impaired dog to thermal radiation. A modified Yerkes discrimination maze was used in which the dogs responded to a stimulus located on one or the other side of the maze. If the dog responded correctly to the stimulus he was rewarded with a small amount of food. Food was withheld from the dogs for 23 hr prior to the test and 1-2 hr after the test. The dogs were conditioned to the maze by using first a buzzer and secondly a visible light which was gradually dimmed by addition to filters until only invisible infra-red radiation was left. These pre-conditioning experiments served to shorten the learning period for the heat stimulus. A standard randomized sequence was used in presenting the stimuli to the animals and generally accepted statistical methods employed in evaluating their responses. More than 10,000 trials were used to determine the threshold of 3 normal dogs; the thresholds at the 75% level of correct choices lay between 0.8 and 13 mc/sec/cm^2. For the dog with grossly impaired temperature regulation the threshold lay between 45 and 55 mc/sec/cm^2 and for a dog with slight impairment of temperature regulation, the threshold lay between 10 and 13 mc/sec/cm^2. Although the operation on the grossly impaired dog undoubtedly had an effect on thermal discrimination, we do not infer from this that it is specifically the damage to the hypothalamus which accounts for the high thermal threshold. (Supported in part by Contract DA-49-007-MD (496) with Office of Surgeon General of the Army.)

DIIODOSULFANILATE LABELED WITH I-131 AS A "γ-RAY SIGNALING COMPOUND" FOR PHYSIOLOGIC STUDIES. William G. Myers. Dept. of Physiology, Ohio State Univ., Columbus.

Development of methods to minimize exposures of human beings to ionizing radiation, when it is deemed prudent to introduce radioisotopes into them in diagnostic or experimental procedures, has become of prime concern to those who strive to heed recommendations made recently by Study Committees of the National Academy of Sciences and the British Medical Research Council. Dynamic studies such as circulation time, cardiac output, radiocardiography, intramuscular or intracutaneous clearance rates, as well as assessments of abnormal placental and fetal physiology in vivo have been achieved in the past by determining changing rates of penetration of γ-rays into suitable detectors placed outside the body during a few seconds or minutes after the injection of ionic radiosodium-24 or serum albumin labeled with radioiodine-131. In these forms, these emitters of γ-ray "signals" are not suitable because they enter metabolic pools, so that their biological half-lives approach the physical half-lives of 15 hr and 8 days, respectively. Consequently, the person is exposed unnecessarily to ionizing radiation during the continuance of the radioactive decay long after the useful information has been derived. Labeling 2,6-diiodosulfanilate with I-131 to specific activities adequate for any purpose is easy to do. The inherent toxicity of the non-radioactive compound is low, and the compound is not known to enter any metabolic "pools" or "spaces." It is cleared from the blood very rapidly by the kidneys to result in a great shortening of the biological half-life of I-131 in this chemical form and a correspondingly lower integral exposure to ionizing radiation.

EFFECT OF HYPOPROTHROMBINEMIA ON TRANSVASCULAR PROTEIN LEAKAGE. Thomas E. Nelson, Jr., Wilfred Cooper and John Clay (intr. by Douglas R. Drury). Dept. of Physiology, School of Medicine, Univ. of Southern California, Los Angeles.

In previous studies in this laboratory we demonstrated an increase in transvascular protein leakage in rabbits given Dicumarol. This effect can be detected within 3 hr after intravenous or intraperitoneal administration, it

appears to precede detectable purpura, and with i.p. injection of the drug a relationship between prothrombin level and protein leakage was obtained. To determine whether this effect of the drug is the result of hypoprothrombinemia or avitaminosis K 2 types of experiment were carried out. One group of rabbits was exposed to carbon tetrachloride to poison liver function, thereby inducing hypoprothrombinemia without producing avitaminosis K, and another group was made vitamin K deficient by biliary fistual. The vitamin K deficient hypoprothrombinemic animals showed an increase in transperitoneal protein leakage above that of sham operated controls but generally less than Dicumarol treated animals, while rabbits treated with carbon tetrachloride showed a decreased protein transfer. These findings suggest that the liver is the principal organ of protein exchange in the peritoneal cavity, that the increased transvascular protein leakage induced by Dicumarol is not caused by the absence of prothrombin but results from interference of the drug with vitamin K activity. (Supported—in part—by grant H-2779 from the National Heart Institute, USPHS.)

FUNCTION OF THE HUMAN FETAL ADRENAL CORTEX. John Nichols. Dept. of Pathology, Med. College of Virginia, Richmond.

There has been much speculation about the function of the fetal zone of the human adrenal cortex but few observations. This part of the adrenal cortex constitutes the major portion of the gland in the newborn infant and which immediately undergoes involution following birth. The most logical suggestion has been that this portion of the gland is associated with sex hormones and is the source of the high 17-KS values known to be present in the new-born infant's plasma. The involution of the fetal zone of the gland parallels the decline in urinary excretion of these hormones. In the anencephalic monster the adrenal is atrophic, the fetal zone being absent. The gland is composed entirely of definitive cortex and medulla. This atrophy is usually ascribed to the absent pituitary and associated absence of ACTH. The purpose of this paper is to report the concentration of 17-OH and 17-KS hormones in maternal and cord blood drawn simultaneously in 5 cases of anencephaly. In all 5 cases the 17-OH levels in cord and maternal blood were within normal limits. Because in these cases the fetal cortex was absent it precludes the possibility that this portion of the cortex forms these hormones. Findings for 17-KS will be reported. One of the 5 cases of anencephaly had a "normal" pharyngeal pituitary and the usual atrophic adrenals. This means that either the pharyngeal pituitary does not secrete ACTH or that other factors are responsible for the adrenal atrophy in cases of anencephaly.

VASO-MOTOR NERVE SUPPLY TO THE PULMONARY BLOOD VESSELS. Yasuyosi Nisimaru, Naotsugu Shinozaki, Tuneji Iizuka and Hirotaka Murakami (intr. by Frederick Sargent II). Dept. of Physiology, Hiroshima Univ. Med. School, Japan.

Although the effects of adrenergic and cholenergic drugs on the pulmonary vascular bed have been investigated, the results following direct stimulation of the automatic nerve supply to the pulmonary blood vessels has not been clearly demonstrated. By using a Ringer solution perfusion technique and recording the effects of stimulation of the sympathetic and parasympathetic nerve supply to the lungs of both the tortoine and bull frog, a measure of the nuero-effector mechanism was observed. The sympathetic nerve effects were produced by stimulating the sympathetic branch at a point proximal to the jugrates ganglion and the vagus effects were recorded by stimulating the parasympathetic branch just before it enters the jugrates ganglion. The observations showed that sympathetic stimulation caused a release of a neuro-effector which was almost identical with adrenaline (Sankyo). The vagus stimulation caused a release of a neuro-effector which was very similar to that produced with acetylcholine.

EFFECTS OF OUTDOOR COLD EXPOSURE ON RENAL FUNCTION IN DOGS. William C. Nungesser (intr. by Benjamin DeBoer). Dept. of Physiology and Pharmacology, Univ. of North Dakota, Grand Forks.

Large trained unanesthetized female dogs of the Labrador strain were exposed to outdoor cold ranging from 0 to -25°C for 1-2 hr. Environmental, rectal and skin temperatures of back and footpads were recorded. Renal functions studied included glomerular filtration rate (GFR), renal plasma flow (RPF), urine volume and osmolality, sodium and chloride excretion. Control experiments to determine the effect of time on the observed functions showed a decrease or no change in GFR, an increase in RPF, decreases in urine volume, osmolality, sodium and chloride excretion and an increase in osmolar urine to plasma (U/P) ratio. When cold exposure followed observations at laboratory room temperature, GFR and RPF increased and the other renal functions listed were either increased or decreased. On the other hand, when cold exposure preceded laboratory room temperature observations, changes in GFR and RPF in the cold were variable, while urine volume, sodium and chloride excretion increased. Urine osmolality and osmolar U/P ratio decreased. In all experiments cold exposure resulted in significant lowering of skin temperatures of back and footpads. No significant change in rectal temperature was seen during exposure to cold of this intensity and duration.

FAST WAVES OF THE DIRECT CORTICAL RESPONSE. Sidney Ochs (intr. by M. Mason Guest). Dept. of Physiology, Univ. of Texas Med. Branch, Galveston.

The direct cortical response (DCR) elicited and recorded from the exposed cortex is a relatively slow positive-negative potential sequence, each phase lasting 10-20 msec. Throughout the positive phase a series of smaller positive-negative waves some 2.0 msec in duration can be observed. These faster "spike-like" responses are identified by their negative peaks. Up to 5 such waves can be distinguished and are labeled F_1 to F_5. The first of these, F_1, begins some 0.3 msec after a 0.1 msec stimulating pulse applied 3-4 mm away. The early onset of the F_1 wave and its positive-negative deflection is consistent with an antidromic propagation up the apical dendrites. Further support for this interpretation came from studies using 2 stimulated regions projecting to a single recording point. Each gave an F_1 response but if the 2nd stimulation was given at the time of the first F_1 wave, the 2nd F_1 wave was occluded. The successive F waves seem to be due to a series of intracortical synaptic discharges between groups of pyramidal cells. The number of successive F groups could determine the duration, and the number of cells in each F group the amplitude of the positive phase of the DCR. This hypothesis is opposed to or may be thought of as operating in addition to post synaptic potential activity on lower soma-dendrites giving rise to the positive phase of the DCR.

FUNCTION OF PHRENIC NERVES IN THE DOG. T. Ogawa*, N. C. Jefferson* and H. Necheles. Dept. of Gastrointestinal Research, Michael Reese Hosp., Chicago, Ill.

Standard textbooks state that the diaphragm is innervated by the phrenic nerves, sympathetic fibers and branches from the dorsal and lumbar nerves. We may assume therefore, that the trophic maintenance of the diaphragm is not entirely dependent on the phrenic nerves. Further, if reinnervation and arborization would occur, the complete destruction of a phrenic nerve should be followed by reinnervation from fibers of the opposite phrenic and from the lumbar and sympathetic nerves. However, our results are at variance with these assumptions. Complete destruction of 1 phrenic nerve leads to complete atrophy of that diaphragm, which begins in the center and progresses toward the parietes (with the possible exception of the posterior leaf). If one phrenic nerve is destroyed, a sharp line of demarkation appears between the 2 anterior leaves of the diaphragm. In 2 experiments there was evidence of innervation of the posterior leaf from the opposite side. On the left side, the nerve divides into 3 distinct branches, anterior, lateral and posterior; when 1 of these branches is destroyed, only the portion of the diaphragm supplied by that branch degenerates. On the right side, the nerve divides in 2 main branches. We have been unsuccessful in demonstrating the so-called 3rd branch which supposedly pierces the

right diaphragm and innervates the celiac and phrenic plexus. One chronic experiment gave evidence of crossed innervation of the right posterior leaf by branches from the opposite side; in 2 acute experiments there was similar but questionable evidence.

ADRENERGIC AND CHOLINERGIC DRUGS AND SPLANCHNIC STIMULATION ON SPLENIC INFLOW AND OUTFLOW. Kenneth Ottis,* Tom Kitchen* and Harold D. Green. Dept. of Physiology and Pharmacology, Bowman Gray School of Medicine, Winston-Salem, N. C.

Blood flow (electromagnetic flowmeter) and pressure were recorded in the splenic artery and vein. The greater splanchnic nerve was stimulated by square waves (15/sec, 15 msec). Epinephrine, arterenol, isoproterenol and methacholine were given in 0.1 μg and 1.0 μg doses intra-arterially and intravenously. Responses to the adrenergic drugs and to splanchnic stimulation were recorded before and after each dose (0.1, 0.3, 1.0, 3.0, 10.0, 30.0 mg.) of the adrenergic blocking drug dibenzyline. The effects of atropine blockade were also studied. Conclusions: the results suggest a) that epinephrine and, to a lesser extent, arterenol induce splenic arteriolar constriction, contraction of the smooth muscle of the splenic capsule and trabeculi and possibly relaxation of the venules; b) that methacholine and isoproterenol, and epinephrine and arterenol during adrenergic blockade induce dilatation of the arterioles; c) that arterenol reversal is more pronounced in the spleen than in any other vascular bed and d) that atropine blocks the dilator responses to methacholine but not those due to adrenergic substances. (Supported by grant H-487, Natl. Heart Inst., USPHS.)

ALTERATIONS IN THE NORMAL GASTRIC FUNCTIONS DURING THE PERIOD OF SPAWNING OF A FISH. T. L. Patterson. California Inst. of Technology, Kerckhoff Marine Lab., Corona Del Mar.

In connection with previous work on the Cabezon fish (Scorpaenichthys marmoratus) attention was focused accidently on the spawning season as to the possibility of its having some influence on the functioning of the gastric mechanism. The fish were stomostomized and each given an individual aquarium where it was free to swim at will. The regular balloon technique was employed to record gastric motility or other physiological data. The results of this investigation shows that the spawning season of this species of fish is comparatively long, ranging from the end of October or mid November and then to January where it reaches its peak and then tapers off at the end of March or mid April. This shows a winter spawning period of about 5 months duration in which there is no evidence of gastric motility. Autopsies revealed that the stomachs of these fishes were contracted and devoid of food, with a very limited amount of fluid probably mostly water. On the termination of the spawning period the gastric motility begins to return, very slowly at first, and then more rapidly until it reaches the state of normalcy.

REVERSAL BY DEGASSING OF CHANGES IN THE PRESSURE-VOLUME CHARACTERISTICS OF LUNGS DUE TO OVER-INFLATION. Solbert Permutt and J. B. L. Howell (intr. by R. L. Riley). Depts. of Environmental Medicine and of Medicine, Johns Hopkins Univ., Baltimore, Md.

Pressure-volume characteristics of normal excised dog and human lungs were measured under relatively static conditions. Following inflation and deflation the lungs consistently contained larger volumes of air at resting volume, the increase being greater with larger inflations, particularly when the duration of the inflation was prolonged. Small inflations to 12 cm H_2O resulted in relatively small increases in resting volume, but large inflations above 20 cm H_2O, especially when maintained for 15-20 min, resulted in as much as 50% of the added volume being retained. Following large and prolonged inflations, the lungs become visibly larger at their resting volumes, and their surfaces were irregular due to scattered, over-inflated regions. Both compliance and the pressure at a given volume were such as to suggest that the lung tissue might have been irreversibly stretched. If, however, an over-inflated lung was

degassed in vacuo to an essentially airless state, then rapidly inflated to 30 cm H_2O, and allowed to deflate to its resting volume, the lung was restored to a state indistinguishable from that existing prior to the over-inflation. These findings indicate that the changes in the pressure-volume characteristics seen following over-inflation were due to reversible mechanical factors and not to irreversible changes in the lung tissue. These results suggest that some of the abnormal pressure-volume characteristics of the emphysematous human lung might be reversible if the over-inflated state were corrected.

CHEMICAL BLEACHING OF VISUAL PURPLE. James C. Peskin. Dept. of Biology, Univ. of Rochester, Rochester, N. Y.

When visual purple solutions are exposed to light, the carotenoid, retinene, is displaced from a photosensitive band and recombines either with amino groups of the visual purple protein or with other free amino groups to form Schiff bases which are pH sensitive. The uniqueness of the photoreaction can be examined by comparison with the effect of chemical bleaching of the photosensitive pigment. Changes in dielectric constant of the visual purple solution by the addition of urea, thiourea or guanidine cause destruction of the pigment in a manner which closely resembles that caused by light. Low concentrations of the reagents have little or no effect on the stability of the pigment, and with greater concentrations the rate and extent of decomposition increases with concentration. The extent of pigment destruction in the several reagents is not only a function of concentration but also of the dielectric constant of the individual compound used. The products which result after chemical destruction of the pigment are identical with those which appear after photo decomposition but the kinetics of the bleaching process are complex and do not correspond to those obtained by photo-bleaching. A similar pattern is shown by treatment of isolated rod distal segments. In this case pigment is destroyed just as in solution, and in addition the destruction can be readily demonstrated as an irreversible process since protracted washing of the treated intact rods removes the urea but does not restore the pigment. Much of this reaction pattern can be interpreted as an alteration of hydrogen bonding in the complex retinene-protein pigment with resulting configurational changes in the molecule. (Supported by Grant B-238 from the Natl. Inst. of Health, USPHS.)

A HOMEOSTATIC MECHANISM OF TISSUE CULTURED CELLS. H. J. Phillips and J. E. Terryberry (intr. by J. R. Johnson). Dept. of Physiology and Pharmacology, Creighton Univ. School of Medicine and Corn State Labs., Omaha, Nebr.

During metabolic studies on Strain L a mechanism was noted whereby cells adjust pH of their environment. Tissue cultures were grown continuously in medium containing 0.25 gm enzymatic yeast and 0.25 gm lactalbumin hydrolysates per liter Earle solution plus 100 ml pooled serum. Cultures were fed 3 times weekly; subcultures were made every 1-1/2 wk; metabolic determinations were made on cells fed the previous day. Suspensions of cells were prepared in ionically balanced phosphate buffered saline. This was done by freeing cells from T-60 flasks with a nylon brush and flushing them through a syringe. The pH of aliquots was adjusted with isotonic monobasic or dibasic sodium phosphate. Viable cells were differentially stained by adding 0.05 ml of 20 mg % Erythrosin B to 1 ml cell suspension. Cell counts were made on a hemacytometer. Lactate was determined chemically after incubation at 37.5°C in 99.9% nitrogen. Determinations were made in pairs: one immediately after equilibration for temperature, the other an hour later. Difference between determinations was taken as lactate formation. Live-dead counts and pH were also determined after an hour. There was no loss of viable cells during 1 hr anerobiosis. Lactate formation increased almost directly with increase in pH. Cells tended to raise or lower pH of medium to 7.2. For example: 6.75-7.00, 6.00-7.14, 7.28-7.26, 7.55-7.40. They lowered pH by increased lactate formation.

CHANGES IN SPECIFIC GRAVITY IN THE FEMALE ALBINO RAT WITH AGE. N. Pordugal* and E. DaCosta. Chicago Teachers College, Chicago, Ill.

The specific gravity of 100 female rats from 6 to 103 wk old, and fed mainly Purina Laboratory Chow, was determined by under water weighings. Separate data was secured on 1) the tail-less, shaved rat, 2) viscera, 3) eviscerated, tail-less rat, 4) skin, and 5) the skinned, eviscerated, tail-less rat. The greatest changes were found in the skinned, eviscerated rats. The lowest specific gravity in this group was 0.9865 found in the 6-wk-old group. An abrupt increase (1.0463) in specific gravity was found in the 8-wk-old, and an irregular increase to 1.0724 in the 22-wk-old rats. In 54 rats between 6 and 22 wk an average specific gravity of 1.0452, with a range of 1.0193-1.0564, was found. At 41 wk the specific gravity was found again to be 1.0724. Then it began to decrease gradually so that at 103 wk it was 1.0363. The average specific gravity of the 19 rats between 42 and 104 wk old was 1.0371. The age between 22 and 37 wk, therefore, represented the highest apparent lean body mass, or least fat, but with the exception of 4 single determinations, the increase in fat with aging was much less in the female than in the male rat.

EFFECT OF BILE ON INTESTINAL ABSORPTION OF CHOLESTEROL-4-C^{14} IN THE RAT. C. Ram Prasad*, R. Suzuki*, Esko Karvinen* and A. C. Ivy. Dept. of Clin. Science, Univ. of Illinois College of Medicine, Chicago.

It was believed that the reports that bile is necessary for the absorption of dietary free-cholesterol in the rat (Siperstein et al., J. Biol. Chem. 198:111, 1952) required a more extensive study than the subject has received. Six chronic bile-fistula rats were prepared. After from 5 to 7 days of absence of bile from the intestine and the daily collection of bile and feces, cholesterol-4-C^{14} was fed with and without oleic acid or olive oil being added to the basal diet. Bile and feces were collected daily for 5-7 days. Less than 1% of the radioactivity administered was excreted in the bile over a period of 4-7 days.

EFFECT OF EPINEPHRINE AND NOREPINEPHRINE ON BILE SECRETION IN UNANESTHETIZED DOGS. E. B. Pratt* and J. H. Holmes. Dept. of Medicine, Univ. of Colorado, School of Medicine, Denver.

Unanesthetized dogs prepared with Thomas-type bile fistulas were given intravenous infusions of the drugs at a rate equivalent to 2 mcgm. of base per kg/min. In 6 experiments during constant Bromsulfalein dye (BSP) infusion, the bile flow showed decreases ranging from 24 to 84% after epinephrine. This was associated with significant increases in bile specific gravity and in concentration of BSP dye, bilirubin and bile acid. All changes were reversed when the epinephrine infusion was discontinued. Similar results were obtained in 3 additional experiments omitting BSP dye infusion and analyses. Three experiments with l-epinephrine bitartrate and BSP infusion yielded identical results. The l-norepinephrine bitartrate, used in 4 experiments, gave inconsistent and insignificant changes in bile volume, specific gravity, and BSP dye, bilirubin, and bile acid concentrations. This demonstrated a fundamental difference in the actions of epinephrine and norepinephrine on bile secretion. This will be discussed from the standpoint of differences in action on metabolism and effective blood supply to the liver.

INFLUENCE OF HYPERCAPNIA ON PULMONARY DIFFUSING CAPACITY FOR CO IN MAN. J. Rankin, R. S. McNeill and R. E. Forster (intr. by J. H. Comroe, Jr.). Dept. of Physiology and Pharmacology, Grad. School of Medicine, Univ. of Pennsylvania, Philadelphia.

Since the pulmonary diffusing capacity for CO (D_L) theoretically varies with changes in the size of the pulmonary capillary bed, it appeared to us to be a good tool for the investigation of the effects of CO_2 on the pulmonary capillaries. Therefore we have measured D_L during hypercapnia in 9 resting normal subjects by the CO - helium breath-holding technique. a) When 10% CO_2 was simply added to the inspired gas mixture used in the measurement of D_L, D_L was

increased an average of 5% and 12% after 10 and 50 sec of breath holding respectively. Pulmonary capillary blood volume (V_c), calculated by the method of Roughton and Forster was measured in 2 subjects and was increased approximately 11%. b) After the subject breathed a gas mixture containing 7.5% CO_2 for 10 min, D_L was increased an average of 24% in all subjects, and V_c was increased an average of 60% in the 2 subjects studied. In 5 subjects repeated measurements of D_L, ventilation rate, systemic blood pressure, pulse rate and pulmonary blood flow (by a single breath acetylene method) were made before, during and after the period of hypercapnia. After starting to breathe the CO_2 enriched gas mixture, D_L rose abruptly, reaching near maximal values in 2-5 min, while the other measurements of respiratory and circulatory phenomena continued to rise for 6-10 min, suggesting that the presumed increase in the pulmonary capillary bed was not directly dependent on the respiratory and circulatory changes.

VASOMOTOR TONE AND EPINEPHRINE REVERSAL. Carlos E. Rapela*, Nathan F. Orovitz* and Harold D. Green. Dept. of Physiology and Pharmacology, Bowman Gray School of Medicine, Winston-Salem, N. C.

The role played by the initial tone of the vessels in the blockade of the epinephrine reversal was studied while recording inflow during constant perfusion pressure in the denervated hind limb muscle in anesthetized dogs. Only a single injection of 10 mg/kg of Dibenzyline was given; this dose had been found to block the dilator as well as the constrictor responses to epinephrine (Youmans et al., Circulation Res. 3: 171, 1955). The Dibenzyline per se increased the conductance (flow/pressure) (av. 340% of control). The first injection of epinephrine (either 1 or 10 μg) within 4-24 min after the Dibenzyline injection always induced a further vasodilatation (av. 170% of the conductance present just preceding the epinephrine). In most instances the conductance failed to return to the pre-epinephrine level. Each successive injection of epinephrine caused a persistent but smaller increase in conductance. By the 2nd to the 5th injection no further increase was induced by the epinephrine, i.e. blockade of the epinephrine reversal appeared to be present. At this time the conductance averaged 560% of that present prior to Dibenzyline. Pitressin reduced this value to 170 and restored the dilator response to epinephrine (av. 220% of the conductance before epinephrine). Conclusion: blockade of the epinephrine dilator response is not due to the dibenzyline per se, but appears to be due to prolonged persistence of the dilation induced by the epinephrine injections following the Dibenzyline. (Supported by Grant H-487, Natl. Heart Inst., USPHS.)

DETERMINATION OF RESIDUAL BLOOD VOLUME NECESSARY FOR SURVIVAL IN RAPIDLY HEMORRHAGED SPLENECTOMIZED DOGS. R. A. Rawson, S. Chien, M. T. Peng, and R. J. Dellenback (intr. by M. I. Gregersen). Dept. of Physiology, Columbia Univ., College of Physicians and Surgeons, New York City.

Immediately following the measurement of blood volume by Cr^{51} and T-1824 in 24 unanesthetized, splenectomized dogs, a rapid hemorrhage (100 ml/min) was performed through a catheterized femoral artery. The percentage dilution occurring after hemorrhage was estimated from changes in percentage plasma proteins, hematocrit and Cr^{51} counts in small arterial samples (1.5 ml) taken at 10, 20, 30, 60, 90, 120, and 150 min post-hemorrhage. At 180 min post-hemorrhage a second injection of T-1824 was given and 4 5-ml samples taken for post-hemorrhage plasma volume determination. Cr^{51} counts were made on all samples and the blood volume estimated at time of maximum dilution, 2nd plasma volume and also at the time of the final sample if indications of hemoconcentration were present. The blood pressure, respiratory rate, heart rate and venous pressure of each dog were recorded pre- and post-hemorrhage with a Sanborn Twin Viso Recorder. The total blood loss in these animals (volume of rapid hemorrhage plus all sample volumes) ranged from 43-55%. Of the 24 dogs, 12 survived, 6 died before completion of 2nd plasma volume, and 6 died between 2-1/2 and 24 hr after the rapid hemorrhage. Of the 10 dogs having

58-62% of their original blood volume remaining, 2-1/2 hr after the rapid hemorrhage, 5 died and 5 survived.

ARTERIAL PRESSURE DECAY FOLLOWING CIRCULATORY ARREST: TECHNIQUE FOR ESTIMATING ELASTIC COEFFICIENT OF A VASCULAR BED. Raymond C. Read,* John A. Johnson, and Hiroshi Kuida*. Depts. of Physiology and Surgery, Univ. of Minnesota Med. School, Minneapolis.

Thirty-six dogs have been perfused with complete cardiopulmonary bypass, using a pump oxygenator. The arterial inflow was interrupted for periods of up to 60 sec with continuing venous outflow. The decay of arterial blood pressure after circulatory occlusion was recorded. This control pattern was compared to that obtained after altering the vasomotor state of the animal with drugs or surgical destruction of the central nervous system. Under these varied experimental conditions, the blood pressure declined steadily with time, no plateau being observed. The initial rate of fall could be approximated by a single exponential expression. Log $p/po = E/R (t - to)$, where E is the overall arterial elastic coefficient (dp/dv) and R is the vascular resistance. From these results mean values for E were calculated and found to vary from 3.3 to 6.6 x 10^5 dynes/cm^5, linearly with the blood pressure (36 - 169 mm Hg).

EFFECT OF ESTRONE ON CARDIAC GLYCOGEN. W. O. Read. Dept. of Physiology and Pharmacology, Univ. of South Dakota, School of Medicine, Vermillion.

The trichloracetic acid (TCA) soluble fraction of cardiac glycogen of female rats falls sharply at approximately 60-70 days of age. Preliminary experiments designed to elucidate the causes of this sharp drop in TCA soluble glycogen shows that estrone administration to ovariectomized 90-day-old rats causes a 70% decrease in the TCA soluble fraction of cardiac glycogen with little change in the TCA insoluble fraction. Adrenalectomy accentuates while hypophysectomy abolishes the effect of estrone. Rats sacrificed following treatment with estrone show a low total phosphorylase activity of cardiac tissue which in part may be used to explain the changes in cardiac glycogen.

EVOCATION OF A RENAL ARTERIOVENOUS INCREASE IN GLUCOSE BY THE ADMINISTRATION OF FRUCTOSE. Roger M. Reinecke and Alejita Firpi*. Dept. of Physiology, Univ. of Puerto Rico, School of Medicine, San Juan.

In a previous study a renal arteriovenous increase in glucose was found to accompany a renal arteriovenous decrease in fructose following the injection of fructose into the rat with ligated ureters (Am. J. Physiol. 186:409, 1956). In order to explore further the causal relation if any of the presence of fructose to the renal arteriovenous increase in glucose, the renal arteriovenous change in glucose was studied following the intravenous injection of fructose, glucose, and saline respectively into the rat with ligated ureters. A statistically significantly greater renal arteriovenous increase in glucose was found following the injection of fructose than following the injection of glucose or saline. The renal arteriovenous change in glucose was then studied following the intravenous injection of fructose and saline and of saline alone into the rat with ligated ureters. A statistically significantly greater renal arteriovenous increase in glucose was found following the injection of fructose and saline than following the injection of saline alone. (Supported in part by Grant A-723 from the Natl. Inst. of Health, USPHS.)

BLOOD AND PLASMA SPECIFIC GRAVITY CHANGES DURING ACUTE ALTERATIONS IN HEMODYNAMICS IN SPLENECTOMIZED DOGS. John W. Remington. Dept. of Physiology, Med. College of Georgia, Augusta.

The role of arteriolar resistance, arterial pressure and venous pressure in quantitatively regulating trans-capillary fluid movement in isolated beds has been determined in other laboratories. A translation into changes in blood and

plasma water as the total peripheral resistance of a whole animal is acutely altered has not been possible. Most quoted studies on capillary exchange are based only on hematocrits, often in animals with intact spleens. Plasma and blood specific gravity determinations were made on simultaneously drawn femoral arterial and venous samples, as the hemodynamics were changed by i.v. infusions of epinephrine, acetylcholine, histamine, plasma or concentrated red cells, and the application of ice. Changes in plasma and blood gravity and in the calculated red cell fraction will be related to those in arterial pressure, cardiac output, total peripheral resistance and central venous pressure. In addition, differences between the arterial and venous blood appear diagnostic. With epinephrine infusion, for example, the plasma specific gravity is sharply elevated, the 1st change being in the arterial blood with a positive A-V gradient. At the end of the infusion there is a rapid fall in plasma specific gravity, arterial blood showing lower values than venous. Derived hematocrit values tend to vary reciprocally with the plasma gravities, indicating possible loss or gain of red cells from peripheral beds. (Supported by Grant H-240 from USPHS, and Life Insurance Med. Research Fund.)

CHANGES IN ACID-BASE BALANCE OF GOAT SERUM DURING GESTATION AND EARLY LACTATION. Monica Reynolds. Dept. of Physiology, School of Veterinary Medicine, Univ. of Pennsylvania, Philadelphia.

This study was undertaken to determine whether an acidosis or an alkalosis exists during pregnancy and early lactation. Each of 5 healthy goats was prepared surgically with a carotid loop. After taking control measurements, 4 goats were bred. At regular intervals throughout gestation and the first 4 wk of lactation, and during the same period for the unbred goat, carotid and jugular blood was drawn. Hematocrit values, pH, using a glass electrode and sensitive temperature control, and plasma total CO_2, by the Van Slyke manometric technique, were determined. Bicarbonate concentration was calculated from the Henderson-Hasselbalch equation. All pregnant goats showed a slight increase in pH and a decrease in CO_2 and HCO_3^- content in the latter part of pregnancy. The values tended to return toward control levels during the first 4 wk of lactation. These results could not be accounted for by changes in environmental temperature or respiratory rate. They indicate the existance of a small, but significant, alkalosis during pregnancy, and complement the findings of other investigators who have observed, in humans, a hyperventilation and a reduced alveolar pCO_2. Additional measurements done on only venous blood but from normal pregnant and lactating cows also show a significant increase in pH and fall in total CO_2. It appears that in these 2 ruminants pregnancy is associated with a respiratory alkalosis which persists for a few weeks post-partum.

EFFECTS OF CONDITIONS OF REST ON RESPONSES TO WORK IN HEAT. M. L. Riedesel*, H. S. Belding and D. M. Ross*. Dept. of Occupational Health, Grad. School of Public Health, Univ. of Pittsburgh, Pittsburgh, Pa.

We (and others) have demonstrated that recovery from exposure to heat is delayed when the recovery environment is warm. An effort is now made to describe the relative costs of doing a hot job in terms of strain and of time required for recovery when recovery conditions are W, "warm," and N, "thermally neutral." A sample study called for performance of 3, 20-min jobs (3 met/hr) under thermal conditions previously established as tolerable (but difficult) for a single half hour. Rest was permitted after each exposure and until heart rate returned to its initial control value plus 5 beats/min. Resting environment was W (96°F, 55% R.H., 100 F.P.M.), or N (86°F, 40% R.H., 100 F.P.M.). The 4 subjects were able to complete the 3 job periods with rest N, but 2 could not undertake the 3rd exposure with W. Heart rate and rectal temperature rose to higher levels when rest W was used. For a representative subject, cost of the effort (3 jobs plus 3 rests) under W was 35% more sweat, 60% more heart beats, 110% more degree x minutes of elevated rectal temperature, 300% more rest time, and 100% more total time. It is concluded: 1) the heart rate index used is not an adequate criterion of unstorage of body heat or

of recovery; 2) strain is markedly reduced and efficiency increased when thermally neutral rest environments are utilized.

EFFECTS OF CHOLINERGIC AND ANTICHOLINERGIC DRUGS ON THE BRAIN ELECTRICAL ACTIVITY OF THE CHRONIC ISOLATED HEMISPHERE RABBIT PREPARATION. F. Rinaldi* and H. E. Himwich. Thudichum Psychiatric Research Lab., Galesburg State Research Hosp., Galesburg, Ill.

The previous investigation of the acutely isolated hemisphere of rabbit's brain revealed slow activity unmodified by cholinergic or anticholinergic drugs (Rinaldi and Himwich, Arch. Neurol. Psychiat. 73:396, 1955). Because such findings might be secondary to the operation which severed the nervous connections but not the blood supply of the isolated hemispheres, these experiments were repeated in animals operated 10 days previously and apparently completely recovered. Again, the electrical activity of the cortex on the isolated side exhibited random bursts of slow waves appearing on a flat background. Sleep spindles and the desynchronization following alerting stimulation failed to appear. While DEP and atropine modified the electrical activity of the isolated cortex, they did so in a manner entirely different from that observed in the intact side. In the isolated cortex atropine did not induce high voltage 14 c/s spindles and DFP did not evoke desynchronized alert activity. It is concluded that the appearance of alert and sleep patterns in the cortex whether spontaneous or induced by the administration of cholinergic and anticholinergic drugs is dependent upon intact connections between the telencephalon and the diencephalon. Histologic check-up revealed the complete separation of the isolated hemisphere from the rest of the brain.

LOCI OF SEX BEHAVIORAL AND GONADOTROPHIC CENTERS IN THE FEMALE CAT HYPOTHALAMUS. Bruce L. Robison* and Charles H. Sawyer. Univ. of California at Los Angeles, and VA Hosp., Long Beach.

The cat ordinarily ovulates only after a complex mating behavior pattern which involves an elaborate after-reaction. The present experiments were designed to determine whether identical or separate hypothalamic centers control mating behavior and the release of pituitary ovulating hormone. With stereotaxic methods under chloralosane anesthesia the hypothalami of more than 30 estrous cats were stimulated bilaterally in one of the following regions: mammillary body, ventromedial nucleus, anterior medial hypothalamus and anterior lateral hypothalamus, in the area of the medial forebrain bundle. At the end of the stimulation (3-5 volts, 30/sec, 5 msec duration, 30 sec on and 30 sec off for 30 min) period, bilateral electrolytic lesions were made at the stimulation sites with the central tips of the bipolar electrodes. Characteristically, ovulation was induced by stimulating either of the 2 posterior but neither of the 2 anterior sites. Similarly, the ventromedial and mammillary body lesions caused ovarian atrophy which led to anestrus, but the cats mated normally if supplied with exogenous estrogen. The anterior lesions left the ovaries in good trophic condition, and they could be ovulated by stimulating the ventromedial nucleus. However, the cats with anterior hypothalamic lesions in either the medial or lateral position repeatedly refused to accept the male even when primed with exogenous estrogen. The results from these combined stimulation and lesion experiments in the female cat indicate that a hypothalamic sex behavioral center lies rostral to and discrete from a tubero-mammillary center controlling the release of pituitary gonadotrophin.

CARDIAC AND METABOLIC RESPONSE OF NON-ATHLETES TO GRADED EXERCISE. E. H. Roorbach*, T. P. K. Lim* and U. C. Luft. Lovelace Fndn., Albuquerque, New Mexico.

The oxygen intake determined during maximal physical exertion is generally accepted as the best objective measure of work capacity. However, such measurements are difficult to obtain on untrained persons and the results are highly dependent on the motivation of the subject. The common observation that the

heart rate increases in linear relationship to the mechanical work load has encouraged attempts to assess the physical competence of an individual on the basis of heart rate and oxygen intake measured at work levels well below the point of exhaustion. The present study is concerned with the cardiac and metabolic response of non-athletes of predominantly sedentary occupations in the 3rd-5th decade to controlled physical activity. Eighty-four healthy males between 22 and 45 years of age performed graded exercise on a bicycle ergometer. The initial work load of 300 mkg/min was maintained for 3 min and then raised by 75 mkg/min each following min. Pulse rate and blood pressure were observed each min and ventilation and gas exchange measured at regular intervals. The test was terminated at the end of the min in which a pulse rate of 180 was attained or exceeded. Since metabolic rate at work varies in proportion to body mass in persons of normal physique, oxygen intake was calculated per kg body weight and plotted against the corresponding heart rate. Statistical treatment of the pooled data revealed good correlation (r = .73) the linearity of which was highly significant. The regression line of oxygen intake/kg b.wt/min (y) on heart rate (x) followed the equation y = .209x−10. Individual performances were rated on the basis of the level and slope of their oxygen intake vs. pulse curve in relation to the regression line.

DEAD SPACE VENTILATION AS A DETERMINANT IN THE VENTILATION-PERFUSION CONCEPT OF RESPIRATORY GAS EXCHANGE. B. B. Ross and L. E. Farhi (intr. by J. M. Brookhart). Univ. of Oregon Med. School and Hadassah Med. Organization, Jerusalem.

Whenever a variation of ventilation perfusion ratios exists among the alveoli of the lungs, the major portion of the end-expiratory dead space gas must have a composition intermediate between those in alveoli having respectively high and low ventilation-perfusion ratios. Therefore, during subsequent inspiration, dead space gas re-entering an alveolus will probably differ in composition from that in the alveolus. For alveoli having a high ventilation-perfusion ratio, this redistribution of dead space gas would have the effect of elevating CO_2 and lowering O_2 partial pressures in a fashion not predicted by the existing ventilation-perfusion equation. It is proposed that the influence of dead space gas composition be accounted for in the ventilation-perfusion equation by including a factor which describeds the average composition of the gas reaching an alveolus from both the dead space and the environment. The equation then becomes a total ventilation-perfusion equation. On a P_{CO_2}-P_{O_2} diagram, this total ventilation-perfusion curve has one origin at the venous point and the other at a point representing the average composition of environmental and dead space gas. The location of this point is determined by the dead space-tidal volume ratio. With this approach, it can be shown that the curve drawn through the venous point and the environmental gas point actually represents the total ventilation-perfusion relationship for a hypothetical lung having no dead space at all.

EXPERIMENTAL CEREBRAL CONCUSSION OF THE RAT. F. Hermann Rudenberg, Thomas W. Jenkins and Sidney R. Govons (intr. by B. B. Alfredson). Depts. of Physiology and Pharmacology, and Anatomy, Michigan State Univ., East Lansing.

We are continuing previous investigations (Govons, J. Neuropath. & Exper. Neurol. 6:95, 1947) regarding the physiology of concussion by studying the physical factors involved in producing unconsciousness. Gentled, unrestrained 90-120-gm rats received a non-lethal, non-fracturing blow upon the head. The missile, which has a flat circular striking area of 3.8 cm^2, descended a wire guide by gravity. To date, weights of 28-110 gm, dropped from 50 to 200 cm, have attained an impact velocity of 3-6 M/sec. Calculations show that neither the momentum nor the force of the missile at impact can be correlated with a knock-out blow. However, a minimum acceleration of about 900 cm/sec^2 and a minimum kinetic energy at impact of about 5×10^6 gm cm^2/sec^2 produce unconsciousness. Daily weight determinations show a correlation between a

knock-out blow and an immediate and transient weight decrease of 2-20 gm lasting 1-2 days. Unconscious rats sometimes have transient convulsions, apnea, and flaccidity; no nystagmus can be elicited. Upon regaining consciousness (15 sec to 15 min after concussion) they manifest a transient mono-, hemi-, or quadriplegia, forelimb adduction, hind limb abduction, circling, tilted-head, and increased docility. About 5 min after regaining consciousness the rats appear normal if undisturbed; defects appear when subjected to motor testing. Little neuropathology has yet been observed in brain sections obtained 2 wk after concussion. Three rats that were unconscious for over 30 min showed motor abnormalities for a number of days and had gross brain lesions.

LEFT VENTRICULAR RESPONSE TO INCREASED "VENOUS RETURN." Robert F. Rushmer, Allan W. Lobb*, Dean Franklin*, and Robert Moss*. Dept. of Physiology and Biophysics, Univ. of Washington, Seattle.

The increase of cardiac output associated with exercise is frequently attributed to an increase in "venous return." Augmented flow into the heart is often induced during controlled experiments on animals by rapid intravenous infusion of blood or blood substitutes in an effort to simulate cardiac compensation to exertion. Changes in left ventricular performance in terms of changes in heart rate, left ventricular dimensions and pressures, rate of change of dimensions, "power" and "work" in intact, unanesthetized dogs have been observed during rapid intravenous infusions, abdominal compression and passive tilting head up and head down. The changes in left ventrifular diastolic pressure produced by these maneuvers failed to induce consistent changes in left ventricular dimensions or energy release. In several instances, an increase in left ventricular diastolic pressure was accompanied by a reduction in diastolic dimensions. These maneuvers failed to reproduce the left ventricular response to exercise, and cannot be regarded as adequate substitutes for spontaneous activity in elucidating normal cardiovascular controls.

EFFECTS OF SUGARS AND OXYGEN ON SWIMMING STRESS IN RATS. Stelios C. Samaras and Nicholas Dietz, Jr.* Depts. of Pathology and Biochemistry, Creighton Univ. School of Medicine, Omaha, Nebr.

We studied the influence of sugars on swimming survival time. As prolonged swimming also increases oxygen requirements, oxygen was administered "tentwise" at regular intervals to certain animals. We used 62 male rats in matched groups. Sugars: in one series, a control was injected subcutaneously with saline, another animal with 10% invert sugar, a 3rd with 50% dextrose. After 15 min the rats were placed into aquaria filled sufficiently to compel continuous swimming until death. Rats injected with 2 cc sugar solutions survived as long as their controls at various (16°-26°C) temperatures. In animals injected with 5 cc portions, survival was 25% longer in the dextrose-injected rats than in the others. In another series, 5 cc dextrose were injected only after marked exhaustion. These rats recovered and swam 2 additional hours, showing up to 6% urinary glucose terminally, whereas saline-injected controls developed convulsions and drowned immediately. All the above types showed terminal albuminuria. Oxygen: enrichment of swimming surface with USP oxygen (7-100 l. during 7-9 hr) did not influence survival time. Higher dosages produced oxygen poisoning convulsions. Rats swimming to exhaustion (8-12 hr at 26°C, nostrils and eyelids bloody, etc.), removed, given oxygen (5 l. in 10 min), revived faster than non-oxygenated controls. Repeated oxygenation speeded recovery. Both types had black, benzidine-positive stools. Forty hours after swimming, autopsy of controls revealed marked pulmonary hyperemia and distention; the oxygenated rats showed only slight pathology. (Aided by American Med. Assoc. grant.)

CHANGE IN IMMUNOLOGIC SPECIFICITY AND MICHAELIS-MENTEN CONSTANT OF MUSCLE ADENYLIC DEAMINASE DURING DENERVATION ATROPHY AND EMBRYOGENESIS. Arthur Samuels (intr. by Clarence A. Maaske). Lab. of Chemical Embryology, Dept. of Pediatrics, Univ. of Colorado Med. Ctr., Denver.

Two rabbit antisera, prepared against electrophoretically homogeneous chicken leg muscle myosin, gave sharp peaks in the quantitative precipitin test and indicated that myosin prepared from embryonic or denervated muscle did not react as completely as normal muscle myosin. Attempts to repeat these experiments with other rabbits gave evidence both by quantitative precipitin and Ouchterlony tests, of at least 2 components in the immunological system. Enzymatic analysis showed that adenylic acid deaminase was present in the myosin preparations and that the several latter antisera which showed broad or multiple peaks in the quantitative precipitin tests inhibited the activity of the ensyme. Control serum did not inhibit the activity nor did the active antisera inhibit the deaminase activity of other species. Therefore the immunological and enzymatic properties of adenylic acid deaminase were studied. It was found that the slope of inhibition at equilibrium obtained when enzyme was incubated with increasing amounts of antisera was about 40% greater for normal adult muscle enzyme than for embryonic or denervated muscle deaminase. Serum absorbed with denervated muscle enzyme inhibited normal muscle deaminase 400% more than either denervated or embryonic muscle when compared concomitantly. An "affinity constant" determined over a wide range of inhibition showed that the normal adult enzyme had a greater "affinity" for the antibody than did the denervated or embryonic form of the enzyme. The Michaelis-Menten constant of the normal adult muscle enzyme determined graphically, from NH_3 liberation data over a 6-fold range of substrate concentration was .5ml/mg or 1.4×10^{-3} l/m while embryonic muscle deaminase km decreased continuously with increasing age from 2.5 at 9 days embryonic age to 0.5 at 15 days. These experiments indicate that the structure of this muscle protein is altered during denervation atrophy and matures during embryogenesis.

CEREBRAL BLOOD FLOW IN THE RAT. Leo A. Sapirstein and Gordon Hanusek*. Ohio State Univ., College of Medicine, Columbus.

Iodoantipyrine (I^{131}) given in a single intravenous injection to the rat shows no change in its distribution between the brain and the remainder of the body between the time of its first recirculation and the end of 1 min. It will be shown that this behavior indicates that the cerebral fraction of the label corresponds to the cerebral fraction of the cardiac output. When data using iodoantipyrine for the cerebral fraction of the cardiac output are combined with data for the cardiac output by dye dilution the cerebral blood flow of the rat is found to be approximately 0.55 ml/gm brain/min, a figure in excellent agreement with that reported for normal man. The cerebral blood flow estimated by this method is shown to increase with the inhalation of 10% carbon dioxide or of 5% oxygen. In both cases, the increase is about 60%. (Supported in part by a contract between the USAF School of Aviation Medicine and The Ohio State Univ. Research Fndn.)

HYPOGLYCEMIC RESPONSE OF THE ADRENALECTOMIZED RAT TO SMALL AMOUNTS OF EXOGENOUS INSULIN AND TOLBUTAMIDE. J. Schiller, V. Liguori* and A. Burks*. Depts. of Psychiatry and Research. VA Hosp., Manhattan, N. Y.

The sensitivity of the adrenalectomized rat to insulin makes of this animal a suitable material for the testing of small amounts of this hormone. Adult female albino rats adrenalectomized for 2 wk or more prior to the test, maintained on 1% NaCL received various amounts of insulin by the intravenous route and the percentage in blood sugar fall was determined. With doses from 0.2 to 0.1 unit a maximum fall of over 60% occurred within 1 hr continued with prolonged hypoglycemia and convulsions. With 0.002 unit the fall was 25.75% at the end of the 1st hr and with 0.001 unit it averaged 20%. Doses of insulin varying from 0.0005 to 0.0001 unit induced a blood sugar fall of 13.5% usually not prolonged after the 1st hr. Parallel responses were obtained with decreased doses of tolbutanide administered intravenously: the fall was of 23.75% with 5.0 mg, of 17% with 1.0-2.0 mg and of less than 10% with 0.02-0.005 mg. The response of adrenalectomized rats to large doses of tolbutamide (25-40 mg. intraperitoneally)

resulted in a hypoglycemic response of a magnitude such as to render inapparent the effect of any amount of added exogenous insulin. In small amounts the effects of the 2 compounds became additive: with 5.0 mg of tolbutamide associated with 0.001 unit of insulin the glycemic fall was 28.6% while with 1.0 mg of tolbutamide plus 0.0005 unit of insulin it was 22.23% that is larger than that of any of the above amounts used separately.

PRESSURE CHARACTERISTICS OF THE ESOPHAGUS AND ITS SPHINCTERS IN DOGS. Jerry F. Schlegel* and Charles F. Code, Section of Physiology, Mayo Fndn. and Mayo Clinic, Rochester, Minn.

Detailed and repeated observations were first made on 2 well-trained, intact, healthy dogs. No anesthetic was employed. Three pressure detecting units, spaced 5 cm apart, were passed orally into the stomach. While pressures were being recorded, the units were withdrawn by stages of 0.5-2 cm through the gastroesophageal junction, the esophagus, and the pharyngo-esophageal junction. Swallowing occurred spontaneously or was induced by the injection of a small volume of water into the mouth, pharynx or esophagus. Distinct bands of elevated pressure were encountered uniformly at the junctional zones. The resting pressure in the esophagus was always below that in the fundus of the stomach. With swallowing, the high pressures in the junctional zones were reduced and a wave of high pressure swept down the esophagus in a peristaltic fashion. Its rate of progression was much more rapid than that previously found in human beings. It is concluded that the esophagus of dogs is guarded above and below by sphincteric bands of muscle which are in a state of tonic contraction during resting conditions and relax during swallowing just prior to the passage of the peristaltic wave of deglutition. As the peristaltic wave reaches the sphincters they contract in peristaltic sequence with the rest of the esophagus. The pressure characteristics of the canine esophagus and its associated sphincters are thus similar to those previously noted in human beings.

EFFECT OF INTRAVENOUS L-NOREPINEPHRINE ON BLOOD VOLUME IN THE DOG. Karl J. Schmutzer*, Ekkehart Raschke*, Samuel A. Marable* and James V. Maloney, Jr. Dept. of Surgery, Univ. of California Med. Ctr., Los Angeles.

Eight years ago, intravenous l-norepinephrine was first shown to be of value in the clinical management of certain hypotensive states. Since that time, however, it has become apparent that sudden withdrawal of the drug after its prolonged administration is frequently accompanied by immediate fall of the aterial blood pressure to such low levels as to endanger the survival of the patient. It is common clinical practice, therefore, to decrease the rate of administration of l-norepinephrine slowly and progressively in an effort to prevent the occurrence of this phenomenon. The purpose of this study is to investigate the underlying causes of this secondary hypotension. In a series of 8 splenectomized, anesthetized dogs, the effect of administration of l-norepinephrine on the blood volume was studied, employing the T-1824 dye method. The determination of the blood volume demonstrated an average decrease of 28.8% after l-norepinephrine (344 mcg/kg/min) had been infused for a period of 90 min. The immediate fall of blood pressure after the sudden withdrawal of the drug was established by control studies and was effectively counteracted by rapid infusion of blood or Dextran (approximately 25% of estimated blood volume). It appears, therefore, that complications encountered after the sudden withdrawal of l-norepinephrine are in large measure due to a decrease in the circulating blood volume.

KINETICS OF THE NEGATIVE AFTER-POTENTIAL IN FROG SINGLE NERVE FIBERS. Gordon M. Schoepfle, Floyd E. Bloom* and Duane Hellam*. Dept. of Physiology, Washington Univ. School of Medicine, St. Louis, Mo.

The negative after-potential of an isolated single nerve fiber is adequately described by the sum of 2 exponential terms with time constants of approximately 10 and 70 msec. Changes in membrane conductance are confined to the brief

initial phase. The magnitude of the entire negative after-potential is a function of membrane potential such that the after-potential/spike ratio is markedly reduced by slight hypopolarization of the membrane. The prolonged terminal phase of the after-potential is characterized by an exponential time constant identical with that of the slow drift in membrane potential associated with break of an anodal pulse. Both phenomena thus appear to involve a change in emf induced by a nonspecific transient change in membrane potential. The time parmeter of this slow drift in emf varies with membrane potential, increasing as the membrane is hyperpolarized. Excess K ion depression of the after-potential is reversible with hyperpolarization of the membrane. As strength of cathodal pulse is increased the slow drift in membrane emf occurring during polarization appears to approach a limiting value at any given instant. The results imply that the prolonged terminal phase of the negative after-potential is simply a change in emf induced nonspecifically by the transient change in membrane potential associated with the spike. (Aided by grant B-173, Natl. Insts. of Health, USPHS.)

MYOCARDIAL DEPRESSION WITH FLUOTHANE ANESTHESIA IN MAN. J. W. Severinghaus, and Stuart C. Cullen*. Div. of Anesthesiology, State Univ. of Iowa, Iowa City.

Arterial hypotension predictably occurs with the administration of Fluothane to man and animals. In man, the pulse slows, pupils are small, skin remains warm and dry, with good color, and capillary refill time is normal with pressures as low as 60/45. It has accordingly been suggested that this hypotension is due to ganglionic blockade. The following experiments suggest, however, that the primary circulatory effect of Fluothane is myocardial depression, with no demonstrable component due to ganglionic blockade in man. Patients were paralyzed with succinyl choline and artificially ventilated with 75% nitrous oxide in an open circuit. One per cent Fluothane was added for 15 min, and the change in cardiac output, arterial and central venous pressure determined. The Fluothane was stopped, the autonomic ganglia were blocked with Arfonad infusion, and the arterial pressure was returned to control levels with an infusion of neosynephrine. After stabilization (45 min), 1% Fluothane was again given for 15 min, and the changes in cardiac output, arterial and venous pressure determined. Before autonomic blockade, 1% Fluothane reduced output 31% and arterial pressure 21% (mean of 4). After blockade, 1% Fluothane reduced output 42% and pressure 40% (mean of 7). Since the circulatory effects of Fluothane were not reduced or eliminated by prior ganglionic blockade, these effects were not due to a sympathetic blockade by Fluothane. Central venous pressure and peripheral resistance rose during Fluothane administration, more in the presence of intact sympathetics. This suggests that myocardial weakening accounts for the major portion of the circulatory depression, and that the sympathetic nervous system tends to compensate partially for myocardial depression due to Fluothane.

FREEZING, THAWING AND FREEZE-DRYING OF BRINE SHRIMP EGGS. J. K. Sherman (intr. by P. R. Morrison). American Fndn. for Biological Research, Madison, Wis.

The object of this investigation is to study lethal factors in freezing, thawing and freeze-drying of living cells. Eggs (early embroys) of Artemia salina are desirable experimental material. They resist drying in nature, inhabit salt water, and provide, in their development into free-swimming larvae, observable criteria of survival. Since dry eggs require 45 min to hydrate, they remain essentially dry for short periods following contact with water. Therefore, dry eggs can be exposed to low temperature in either air or water. In a series of experiments, dry and wet (hydrated) eggs, in air and water, were cooled to and rewarmed from temperatures above and below freezing at various rates. In other experiments, dry and wet (hydrated) eggs were frozen-dried. Findings include: 1) eggs, dry or wet, are unaffected by rapid rates of cooling above freezing temperatures; 2) dry eggs survive (100%) freeze-drying and subsequent

storage for at least 2 months at room temperature; 3) dry eggs survive (100%) cooling to and rewarming from -78 and -196°C at various rates; 4) wet (hydrated) eggs show loss (10-97%) during freezing and thawing; percentage survival increases with increased rates of freezing and thawing, and is better in air than in water; 5) freeze-drying of wet eggs is lethal to all but a few (<1%). Over-all findings suggest that physical injury by ice is a possible lethal factor in freezing and thawing of hydrated brine shrimp eggs. Also, death on freeze-drying may occur during drying and/or reconstitution as well as during initial freezing.

DIFFUSING CAPACITY OF DOG'S LUNGS. A. A. Siebens, R. A. Rauf* and Louise Ray*. Dept. of Physiology, State Univ. of New York, Downstate Med. Ctr., Brooklyn.

The method of Lilienthal and Riley was used in making 25 measurements of pulmonary diffusing capacity for oxygen in 10 full-grown anesthetized dogs. The dogs were suspended upright in a partly crouched position from a hammock through which the extremities protruded. Exercise was produced by delivering pulses of 60-cycle current to the extensors of the semi-flexed limbs. There resulted a caricature of normal jumping, variable in frequency and magnitude. Valves for oxygen consumption ranged from 26 to 47 cc O_2/min/kg. Blood samples from right ventricle and carotid artery were analyzed for gas tensions by the bubble equilibration technique. The Scholander apparatus was used in measuring the composition of expired air. Exercise was continued over a period of 10 min before samples were collected. At the lower level of oxygenation, the tension of oxygen in arterial blood was 43 mm Hg or less. The mean alveolar-capillary oxygen tension gradients ranged from 25 to 44 mm Hg. The mean of the 25 diffusing capacities was 17.7 with a standard deviation of 4.1. The diffusing capacity per kg of body weight was .97±.13 and per m^2 of body surface area was 22.8±3.4. Comparable values in 12 exercising young men are 74.9±6.1, 1.03±.09, and 39.7±3.4. If one assumes that dog and man alveolar capillary membranes have comparable thickness and permeability, the close agreement only between figures for diffusing capacity per kg suggests that the alveolar capillary beds of these exercising mammals differ in area during the physically active phase of life as a function of body mass rather than of body surface area.

RELATIVE IMPORTANCE OF PLASMA BICARBONATE CONCENTRATION AND ARTERIAL pCO_2 IN THE REGULATION OF RENAL ACID EXCRETION. Daniel H. Simmons, Nicholas A. Assali, and Melvin A. Avedon. (intr. by M. I. Grossman). VA Ctr. and Univ. of California Med. Ctr., Los Angeles.

Both plasma bicarbonate concentration and arterial pCO_2 have been shown to be related either to the rate of renal acid excretion or to the rate at which tubule cells secrete hydrogen ions. This study is concerned with work on the relative importance of these 2 blood factors in determining the rate of urinary acid excretion. Proportional changes in bicarbonate and pCO_2 were induced by holding arterial pH constant while altering the acid-base status of 11 anesthetized dogs. Following 3 30-min control periods, intravenous infusions of 0.15 M HCl or sodium bicarbonate (0.3 ml/min/kg b. wt.) were started and progressive acid-base alterations induced. Arterial pH, and therefore the ratio of bicarbonate and pCO_2, was kept constant (within 0.03 pH units) by frequently adjusting ventilation, alveolar pCO_2, and arterial pCO_2 with a variable-stroke Starling respiration pump. Changes in blood bicarbonate and pCO_2, and changes in the rate of renal acid excretion (the sum of urinary ammonia and titratable acid) were then followed during 3 subsequent 30-min periods. Since parallel changes in plasma bicarbonate and in arterial pCO_2 have opposite effects on acid excretion, the relative importance of the 2 blood factors should be reflected in the direction of the change in acid excretion. Of 28 clearance periods observed following infusion of acid or base, acid excretion changed in the direction expected from the changes in bicarbonate in 25, while acid excretion changed in the direction predicted by changes in pCO_2 in only three. This implies that changes in plasma bicarbonate have more effect on the regulatory mechanism of urinary acid excretion than do proportional changes in pCO_2.

EFFECT OF EPINEPHRINE ON LIVER GLYCOGEN. Joseph E. Sokal and Edward J. Sarcione (intr. by Clarence Peiss). Div. of Medicine, Roswell Park Memorial Inst., Buffalo, N. Y.

Our current teaching of the subject of epinephrine action on glycogen stores is based in part on several hypotheses which have never been subjected to experimental test. It appeared worth-while, therefore, to attempt a critical review of this subject. Certain of the classic experiments have been repeated. Route of administration, experimental conditions and dosage of epinephrine have been varied. Major attention was devoted to the design of experiments which would test the hypotheses which appear to have been accepted on inadequate grounds. Among the conclusions we have reached which are at variance with current teaching are the following: 1) high blood lactic acid levels exert only a minor effect on the liver glycogen; with proper stimulation, hepatic glycogenolysis will take place in spite of an intense "flood" of lactic acid from muscle which should "force" net synthesis of liver glycogen. 2) The mechanism of action of epinephrine is unknown. We do not deny that epinephrine converts inactive phosphorylase to the active form. This must, however, be a side-effect of epinephrine; it cannot account for its observed effects on glycogen metabolism.

EFFECT OF PERFUSION PRESSURE ON THE "CIRCULATING VOLUME" OF THE ISOLATED CANINE KIDNEY PERFUSED WITH A KEROSENE-MINERAL OIL MIXTURE. Jin Min Soo and Irving Green (intr. by Philip Dow). Dept. of Physiology, Med. College of Georgia, Augusta.

Canine kidneys were removed and treated for kerosene-mineral oil perfusions according to the method of Waugh (Rochester Meeting, 1956). Injections of Sudan IV were made at zero time into the renal artery through a 26-gauge indwelling needle. The perfusion medium was collected in tubes passing at constant speed on a kymograph and the concentrations of dye were determined by Beckman spectrophotometry. Collections were made at perfusion pressures ranging from 60 to 200 mm Hg. The pressures were first raised by approximately 40 mm increments and then lowered back to the starting pressure in the same manner. Recovery of dye was essentially complete since directly measured and calculated flow always agreed well within 10%. The volume of circulating fluid was calculated from the product of flow times mean transit time. Both parameters were determined from the plot of concentration vs. time. The expected increases in circulating volume at elevated perfusion pressures were not obtained. On the contrary, there was either no change at all or there occurred a decrease in circulating volume. When the pressure was reduced a profound increase in volume resulted. (Supported by grants from the Natl. Heart Inst. and the American Heart Assoc.)

SOME FACTORS REGULATING UNESTERIFIED FATTY ACID TRANSPORT. John J. Spitzer, Judy A. Spitzer* and Harvey I. Miller*. Dept. of Physiology, Hahnemann Med. College, Philadelphia, Pa.

Rat adipose tissue, lung, pancreas, heart and striated muscle caused lipolysis of cotton seed-oil emulsion in vitro with the appearance of unesterified fatty acids. Liver was ineffective. Heparin (0.2 mg/ml) increased lipolysis by adipose tissue and heart in most experiments but failed with the other organs. Sodium desoxycholate (5.0 mg/ml), although increasing lipolysis by pancreas, had no effect on the enzyme activity of adipose tissue and heart. Protamine (0.1 mg/ml) failed to inhibit lipolysis by adipose tissue and heart. These findings are consistent with our previously reported results regarding the in vivo production and transport of unesterified fatty acids (3rd Internat. Conf. on Bioch. Problems of Lipids, 1956). In dogs, histone (2.5-5.0 mg/kg) influenced lipid transport in vivo in the same manner as protamine. In lipemic dogs, histone increased lipemia without affecting the unesterified fatty acids. In similar animals after heparin, histone reversed the action of heparin, increasing lipemia and decreasing clearing activity of the plasma and decreasing unesterified fatty acids. In nonlipemic dogs, it failed to influence unesterified or esterified fatty acids, reversed the action of heparin on clearing activity and

opposed the elevation of unesterified fatty acids. These results and the fact that histones are widely distributed in the body, suggest a possible physiological function for histones in regulating unesterified fatty acid metabolism. (Supported by the Natl. Heart Inst., USPHS.)

EFFECT OF EPINEPHRINE, NOREPINEPHRINE AND SEROTONIN ON PROPULSIVE MOTILITY OF RAT SMALL INTESTINE. J. Clifford Stickney, David W. Northup and Edward J. Van Liere. Dept. of Physiology, West Virginia Univ. Med. Ctr., Morgantown.

Propulsive motility of the small intestine was determined in adult female albino rats of the Wistar strain weighing on the average 160 gm. Two ml of a charcoal suspension in aqueous gum acacia solution was introduced by gastric intubation, and the rats were killed 20 min later for removal of the small intestine and measurement of the length traversed. Groups of 10 rats each were used for the study of each agent or of saline. At the time of intubation, saline, epinephrine (20 mcg/kg), an equivalent dose of norepinephrine (18 mcg/kg) or of serotonin (1 mg/kg) were injected intraperitoneally at random. The percentage of the intestine traversed was 65, 29, 50 and 46 respectively. In the doses used all the agents caused a statistically significant reduction in motility. Epinephrine caused a greater reduction than either its close relative norepinephrine, or serotonin.

EFFECT OF PENTOBARBITAL ANESTHESIA ON Tm_{PAH} IN THE DOG. E. J. Storen (intr. by E. Lovell Becker). Surgical Research Lab., Med. College of Virginia, Richmond.

Glauser and Selkurt (Am. J. Physiol. 168:469, 1952) observed no appreciable depression of Tm_{PAH} in dogs anesthetized with pentobarbital when the experiments lasted less than 3 hr. In our studies, pentobarbital caused a marked depression of Tm_{PAH} in dogs as early as 1-1/2 hr after the induction of anesthesia. No significant alterations were found in glomerular filtration rate, effective renal plasma flow or in filtration fraction. In 6 normal female mongrel dogs with both kidneys explanted to a subcutaneous position, 12 experiments were done with anesthesia, and 12 experiments were done without anesthesia. Each experiment included 3 urine collection periods at low plasma levels of PAH, and 6 at Tm levels. No experiment was longer than 3 hr. The mean value of Tm_{PAH} in 6 unanesthetized dogs was .743 mg/min/kg body weight (S.D. $\pm$.081), while in the anesthetized animals Tm_{PAH} was .546 mg/min/kg body weight (S.D. $\pm$.035), with a p value below .02. The Load/T ratios in these experiments had been kept at low levels to avoid self depression of Tm_{PAH}, as this was a consistent occurrence in the anesthetized animals at Load/T ratios above 4. Renal extraction of PAH was measured in 2 unanesthetized and in 6 anesthetized animals by percutaneous puncture of the renal vein. The results agreed with accepted values.

BEHAVIOR AND ITS MODIFICATION BY LESIONS OF THE AMYGDALA AND RELATED PROJECTION SYSTEMS. Thomas B. Summers and William W. Kaelber (intr. by H. M. Hines). Depts. of Neurology and Anatomy, Univ. of Iowa College of Medicine, Iowa City.

Abnormal behavior following destructive lesions in the region of the ventromedial hypothalamic nuclei is a frequent finding in the cat. Ferocity or savageness of varying degree will be seen in 25-40% of such animals. Destructive lesions elsewhere in the upper brain stem and adjacent temporal lobes have produced conflicting results as reported by various investigators; results have been equally antithetical in regard to the reversibility of the savage state. In view of these findings it was felt that a reappraisal of this problem was in order. Using the cat as the experimental animal, the authors have produced bilateral destructive lesions in the amygdala by surgical extirpation, necrosis and other means. These animals have shown no behavior change as previously defined. Animals rendered savage by destructive lesions in the ventromedial nuclei of the hypothalamus were subjected to subsequent destruction of the amygdala and

dorsomedial hypothalamic nuclei. In addition, an attempt has been made to explore other regions, involvement of which might either mimick or modify the behavioral change observed in the hypothalamic preparations.

MINIMAL DYNAMIC RESPONSE REQUIREMENTS OF MANOMETER SYSTEMS FOR RECORDING LEFT ATRIAL AND VENTRICULAR PRESSURES IN MAN. William F. Sutterer*, H. J. C. Swan and Earl H. Wood. Mayo Clinic and Mayo Fndn., Rochester, Minn.

Left atrial pulses were recorded through a special 18T needle assembly around a small-bore catheter threaded through this needle and used for simultaneous recording of left atrial or ventricular pressure. Output of the cathether manometer was recorded in rapid succession by galvanometers of widely different dynamic response, while simultaneous pulses via the left atrial needle served as a base line for study of the effect on the recorded left atrial pulse. Effects on recorded ventricular pulses were studied, with the aortic pulse during systole and left atrial pulse during diastole for comparison. Dynamic response of the systems to square and sinusoidal pressure changes was determined with a hydraulic oscillator. The needle system maintained its sensitivity above 90% of static response out to 45 cycles per second (cps), and the 3 catheter systems to 3, 9, and 25 cps, respectively. Simultaneous atrial pressures by the 45 and 9 cps system were not significantly different; however, peak A, C and V wave pressures by the 3 cps system averaged less by 1.5, 1.5 and 1.0 mm Hg, respectively. The delay of the V wave peak averaged 0.025 and 0.056 sec for the 9 and 3 cps systems, respectively. Peak ventricular systolic pressures and end diastolic pressures were not different for the 3 systems. Systems for recording left atrial and ventricular pulses in man should maintain a uniform sensitivity from 0 through 9 cps or above.

EFFECT OF ORAL MARSILID ON GASTRIC SECRETORY RESPONSE TO A MEAL. R. Suzuki*, H. B. Hays* and A. C. Ivy. Dept. of Clin. Science, Univ. of Illinois College of Medicine, Chicago.

Marsilid (l-isonicotinyl-2-isopropylhydrazine) is an inhibitor of mono-amine oxidase. It is a drug given orally in tuberculosis, in which disease it increases appetite, and elevates the mood and perhaps by increasing the serotonin content of the brain. Given slowly intravenously to dogs it has been found to stimulate the secretion of the fasting stomach probably by its mono-amine oxidase activity (Ivy et al., Am. J. Physiol. 186:239, 1956). In this study four Heidenhain pouch dogs were used. The test-meal consisted of 100 gm Pard (Swift & Co.) in 200 cc water. The test-meal was fed 11 times daily without Marsilid administration, as a control. Then Marsilid in a dose of 50 mg was given orally at 7:30 a.m., 2:00 and 9:00 p.m. on successive days, the test-meal being repeated 10 times during this period. Then Marsilid was stopped, and 10 test-meals were fed on successive days. The output of HCl was decidedly increased during the period of Marsilid administration.

FACTORS INFLUENCING ACTIVE EXPIRATION IN DECEREBRATE CATS AND APNEUSTIC BREATHING IN PONTINE DECEREBRATE CATS. Pei Chin Tang. Dept. of Physiology-Biophysics, School of Aviation Medicine, USAF, Randolph AFB, Texas.

Phrenic discharge was recorded from phrenic branch of 3rd cervical nerve without pneumothorax and displayed on Sanborn recorder after integrated with simple capacitor-resistor circuit. Integrated phrenic discharge closely resembled pattern of abdominal movements recorded with mercury-in-rubber strain gauge. Intra-abdominal pressure was recorded with rubber balloon and strain gauge. Tracheal pressure was recorded with strain gauge to indicate roughly gas flow rate. Intercollicular decerebrate cats showed no active expiration as indicated by no intra-abdominal pressure rise during expiration. Breathing 5% or 7% CO_2 in oxygen resulted in progressively increased active expirations along with usual increase in breathing rate and amplitude. Breathing 10% oxygen in nitrogen resulted in increased breathing rate and amplitude with

occasional ill-defined active expirations. Following vagotomy, amplitude of active expirations in response to CO_2 breathing became several times larger than that of control indicating that vagal impulses inhibit active expiration. During apneustic breathing following combined vagotomy and pneumotaxic center ablation, active expirations often appeared spontaneously. Artificial hyperventilation gradually reduced and finally abolished these active expirations suggesting that hypercapnia may play important role in apneustic breathing. Prolonged hyperventilation shortened and finally abolished inspirations. After changing from air to 7% CO_2 in oxygen while continuing hyperventilation, inspirations re-appeared and became progressively longer in duration and greater in amplitude indicating CO_2 being an important factor in producing inspiratory spasms. Gasping appeared to be result of hypoxia because hyperventilation with 5% or 7% CO_2 in oxygen abolished gasping though not inspiratory spasm during apneustic breathing.

DISCRIMINATION BETWEEN INTERMITTENT PHOTIC STIMULATION AND A STEADY LIGHT IN THE CAT. Charles L. Taravella*, George Clark, Eugene L. Pautler*, Allen C. Norton* and Arthur Schwartz*. Depts. of Physiology and Psychology, Univ. of Buffalo, Buffalo, N.Y.

Five cats were trained to make a discrimination between a flickering and a steady light. As learning progressed, the rate of flicker was progressively increased until 65 flashes/sec was reached. All cats were finally able to make this discrimination after 1500-2500 trials. The learning curves were characterized by plateaus (one or more) followed by short periods of rapid improvement. All control procedures were negative. After reaching criterion (80% correct on 3 consecutive days) the animals were subjected to bilateral ablations of selected portions of the cerebral cortex. In 1 animal an attempt was made to remove only the striate cortex, in 2 animals the lesions were extended rostrally and laterally from the striate cortex while in the remaining 2, the gyrus marginalis, gyrus suprasylvius and gyrus compositus posterior were all ablated. The first 2 groups of animals were able to relearn the discrimination to the preoperative level after about 3500 trials while in the 3rd group with much larger lesions there was virtual retention of the discrimination.

EFFECTS OF RHINENCEPHALIC LESIONS ON MAZE LEARNING IN THE RAT. Garth J. Thomas and Leon S. Otis (intr. by Leo G. Abood). Research Labs., Neuropsychiatric Inst., Univ. of Illinois, College of Medicine, Chicago.

This experiment was done to see if rhinencephalic lesions which we had previously shown to interfere with conditioning of avoidance responses would have a similar effect on maze learning. Maze learning supposedly is less dependent on "emotional" factors than is avoidance conditioning. Twelve rats sustained electrolytically induced lesions in a stereotaxic instrument aimed at the rostral region of the hippocampus. Twelve control animals suffered only small cortical lesions. After recovery from the operations the animals were tested for learning ability in a Lashley 8-cul maze. The experimental rats showed significantly defective learning compared with the controls in terms of trial to criterion, errors, total time of learning, and trial of first errorless trial. The groups did not differ significantly in time of the first trial. Histological study of the brains showed that the experimental lesions involved more than the hippocampus. The cortical fiber layer was invaded and the corpus callosum damaged. Also cortical projection fibers from anterior thalamic nuclei were interrupted as indicated by retrograde degeneration. Definitive conclusions cannot be made regarding critical characteristics producing the behavioral loss, but interruption of projection fibers from the anteroventral thalamic nuclei to the cingulate cortex is interpreted as the most likely cause of the impaired maze performance. It is tentatively suggested that the lesions produce the impairment through interference with mechanisms of secondary motivation.

PRIMARY AUDITORY STIMULUS GENERALIZATION AS A FUNCTION OF ACQUISITION LEVEL IN THE CAT. Richard F. Thompson (intr. by C. N.

Woolsey). Lab. of Neurophysiology, Dept. of Physiology, Univ. of Wisconsin Med. School, Madison.

The present experiment investigated primary stimulus generalization in the cat, as a function of level of acquisition. Auditory stimuli of various frequencies were employed. All animals were conditioned with a 250 cps tone to 20%, 55%, or 90% acquisition levels (percentage response in a block of 20 trials) and then extinguished at 250, 500, 1000, 2000, 4000, or 8000 cps to a criterion of 20 responseless trials. The animals extinguished at 250 cps served as the control group for measures of relative generalization. The animals were conditioned to give a running response in the Brogden-Culler rotary conditioning apparatus. Using number of trials up to and including the first response failure in extinction, and number of responses in the first 20 extinction trials as measures, total number of responses tended to decrease with increasing generalization text frequency, and to increase with increasing acquisition level, for frequencies close to the training tone. For relative generalization, the above 2 measures were employed by dividing the individual experimental group scores by the control group (250 cps) means. Relative generalization was found to increase from the 20% to the 55% acquisition levels, and then to decrease at the 90% level for 500 and 1000 cps test frequencies, to be inversely related to acquisition level for 2000 and 4000 cps test frequencies, and to be zero for all acquisition levels for 8000 cps test frequency. The overall generalization gradient, plotted in terms of jnd's, was a linear decreasing function of generalization test frequency. (Supported by the Natl. Inst. of Neurological Diseases and Blindness, USPHS, Grant B-896.)

DECREASES IN INTESTINAL ABSORPTION OF A SODIUM CHLORIDE SOLUTION PRODUCED BY SUBSTITUTED PHENOLS WHICH UNCOUPLE PHOSPHORYLATION. C. S. Tidball, D. A. Schoenstadt, and M. E. Tidball (intr. by J. O. Hutchens). Dept. of Physiology, Univ. of Chicago, Chicago, Ill.

The influence of substituted phenols on absorption from a 1% NaCl solution in isolated jejunal loops was studied in acute experiments on 15 dogs anesthetized with sodium pentobarbital. The method has been described previously (Tidball and Tidball, Am. J. Physiol. 185:313, 1956). The substituted phenols with varying ability to inhibit oxidative generation of high energy phosphate bonds were added to the 1% NaCl test solution so that a $1x10^{-3}$M concentration of the derivative resulted. When $1x10^{-3}$M 2,4,5-trichlorophenol (TCP) was used, the net absorption during each of 3 consecutive 10-min test periods was significantly decreased. When 1% NaCl was reinstated as the test solution the net absorption promptly returned to control level. Similar reversible effects were obtained with 2,4-dinitrophenol. Protein analyses of material returned from a loop after each 10-min test period was made and the values used as an index of relative secretion. Although small increases in secretion were seen in some experiments, the predominant change was a decrease in true absorption. When $1x10^{-3}$M 2,6-dibromophenol (DBP) was present in the test solution, no changes in net absorption or secretion occurred. DBP has only one one-hundredth the activity of TCP in inhibiting functions dependent on aerobic phosphorylation (Krahl, Biol. Bull. 98:175, 1950). The decrease in absorption is therefore attributed to an uncoupling of phosphorylation reactions. These results are consistent with a hypothesis that an active transport system utilizing energy via high energy phosphate linkages plays a part in the intestinal absorption of water and salts.

CARDIO-PULMONARY RESPONSES TO NEGATIVE PRESSURE BREATHING IN MAN. Er-yi Ting*, Suk Ki Hong* and Hermann Rahn. Dept. of Physiology, Univ. of Buffalo School of Medicine, Buffalo, N. Y.

The cardio-vascular adjustments and pulmonary mechanics have been studied on subjects continuously breathing into a large box, the pressure of which is maintained at 20-30 cm H_2O below atmospheric pressure (negative pressure breathing). This maneuver is equivalent to being submerged horizontally under water to a depth of approximately 25 cm while breathing through a rigid tube. The vital capacity was reduced to 80% and the expiratory reserve volume to 26%.

The minute volume increased approximately 50%, due to an increase in breathing frequency. The airway resistance was almost doubled at a flow rate of 1 l/sec, while the lung compliance was reduced to 50%. Both the systolic and diastolic pressure and the heart rate were not altered significantly. Finger plethysmography provided evidence for peripheral vasoconstriction. The intrapleural pressure (esophageal balloon method) follows closely the negative intrapulmonary pressure. Thus, the heart, pulmonary vessels and intrathoracic veins are exposed to greatly decreased pressures. However, the peripheral venous pressure changes little, due to a collapse of veins entering the thoracic cage. It is proposed that this venous collapse serves as defense mechanism for maintaining normal peripheral circulation pressures and preventing pulmonary congestion. The extra strain on the circulation is placed on the left heart which has to overcome the induced negative pressure.

CHARACTERISTICS OF AN ANTITHROMBOPLASTIN ISOLATED FROM MAMMALIAN TISSUES. Eugene J. Towbin (intr. by Samuel A. Corson). Dept. of Medicine, Univ. of Arkansas and VA Hosp., Little Rock.

Additional work with the material described by Fisch and Towbin in Fed. Proc., 8, 45, 1949, reveals the following: acid extraction and ammonium sulphate precipitation of a wide variety of tissues yields an active but crude protein material. Electrophoretic and cold ethanol solubility characteristics of the antithromboplastin will be described. The material does not inactivate convertin or antihemophilic globulin. However, it inhibits the generation of convertin and thromboplastin from their precursors. Crude PTC preparations partially inhibit this anticoagulant and appropriate concentrations of platelets, crude or heated brain or lung thromboplastins and trypsin all completely inhibit its effects.

PREVENTION OF HYPOTHERMICALLY INDUCED CARDIAC FIBRILLATION BY CONSTANT INFUSION OF NOREPINEPHRINE. J. K. Turner and F. R. Mugler, Jr. (intr. by A. D. Keller), Physiology Dept., U. S. Army Med. Research Lab., Fort Knox, Ky.

Progressive hypothermia was induced in Nembutalized dogs by blood stream-cooling. In an untreated group of 12 animals ventricular fibrillation occurred without exception at a mean deep colonic temperature of 25°C. In a norepinephrine-infused group of 16 animals the hearts did not fibrillate and arrest supervened at a mean temperature of 17°C. In a 3rd group of 5 animals fibrillation was precipitated, the hearts were defibrillated by a closed chest procedure and the animals permanently resuscitated. Several weeks later hypothermia was again induced during continuous infusion of norepinephrine. During this induction 1 heart fibrillated at a temperature 6°C below the original fibrillation. In the others, arrest supervened at a mean temperature 6°C below the untreated fibrillating levels.

SUCCINOXIDASE ACTIVITY OF AGED AND DAMAGED BRAIN, LIVER AND HEART PREPARATIONS. David B. Tyler. Schools of Dentistry and Medicine, Univ. of Puerto Rico, San Juan.

Mitochondria prepared from intact and damaged tissues homogenized in 0.23 M sucrose containing .001 M EDTA and Tris buffer were assayed for: 1) succinoxidase activity; 2) the ability of oxaloacetate to inhibit this activity; 3) the effect of ATP and magnesium to counteract the oxaloacetate inhibition; 4) the capacity to utilize added oxaloacetate; and 5) the effect of added calcium on these activities. The results indicate that both damaging (anoxia) and aging the brain tissue increases the succinoxidase activity. This increase is not consistently associated with decreased endogenous production of oxaloacetate. Also, the succinoxidase system shows an increased sensitivity to the inhibitory action of added oxaloacetate. There also occurs a decrease in the capacity of such damaged tissue to form complexes of ATP, magnesium and oxaloacetate, described previously (J. Biol. Chem. 216,395, 1955) and to utilize added oxaloacetate. Added calcium activates the succinoxidase activity of Versene prepared

mitochondria. This "activation" is also not consistently accompanied by a decreased endogenous oxaloacetate production nor can it be satisfactorily explained by "surface" or permeability changes. Tissue differences in the above effects are principally quantitative. (Supported by grants from the Natl. Insts. of Health, USPHS, and Life Insurance Med. Research Fund.)

SODIUM DIFFUSION IN RESTING AND STIMULATED RAT BRAIN; CORRELATION WITH PROTEIN STRUCTURE. G. Ungar and D. V. Romano*. Dept. of Pharmacology, U. S. Vitamin Corp., New York City.

It has been shown that electrical stimulation of the brain through afferent nerves produces protein changes similar to denaturation, as indicated by an increase in the ionized side-groups of tyrosine and cysteine (J. Gen. Physiol. 40:635, 1957). It was suggested that such modification of protein structure may affect the affinity of cells for K^+ and Na^+. To explore this possibility, extracts of rat brain, frozen in the resting and stimulated state, were submitted to diffusion studies. Diffusion of K^+ and Na^+ into distilled water was measured for varying periods in a system where the brain extract was separated from the solvent phase by a cellophane membrane. At equilibrium no significant difference was observed between resting and stimulated tissue. During the 1st hour, however, diffusion of Na^+ was consistently slower from stimulated brain ($D = 1.08 \pm 0.027$) than from the resting tissue ($D = 1.23 \pm 0.025$). Without extract, the diffusion coefficient of NaCl under the same conditions was 1.33. The diffusion system was standardized by means of the usual value of $D_{KCl} = 1.63$. Diffusion of K^+ was not found significantly altered by electrical stimulation. Decrease in sodium diffusion shows a high correlation with side-group ionization (measured spectrophotometrically) and free -SH groups (measured by amperometric titration). The influx of Na^+ during excitation may therefore be related to an increased affinity of cell proteins for this cation.

ELECTROENCEPHALOGRAPHIC ANALYSIS OF INSULIN HYPOGLYCEMIA BASED ON COMPARATIVE RESPONSES OF CORTICAL AND SUBCORTICAL AREAS. William G. VanMeter*, Helen F. Owens* and Harold E. Himwich. Thudichum Psychiatric Research Lab., Galesburg State Research Hosp., Galesburg, Ill.

In order to follow the course of insulin hypoglycemia in the brain, New Zealand albino rabbits weighing approximately 3.0 kg were fasted for 24 hr and 10 units of protamine zinc insulin injected the night prior to the experiment. Forty units of regular insulin were injected i.m. hourly during the experiment. Minimal pentobarbital anesthesia was used, when necessary, to prevent convulsions. Artifical respiration was employed. Bipolar electrodes were implanted and recordings were made from the right and left motor, limbic and occipital cortical areas; and the right and left hippocampal, amygdalcid and midbrain areas. Pain stimulation was produced by pinching the hind leg and visual stimulation by a photostimulator. Electrical potentials become slower and of lower amplitude before they disappeared. The cortical potentials usually disappeared prior to those of the subcortex. Seizure-like waves developed either before or after disappearance of spontaneous electrical potentials. Seizure waves can appear in all leads simultaneously or may be restricted to the subcortex, chiefly the hippocampus and/or amygdala. Tonic and clonic convulsions appeared intermittently throughout the recording. The alerting response to pain was extinguished prior to that of the occipital cortex to visual stimulation. The response to photostimulation persisted in the midbrain after the spontaneous and evoked potentials were no longer present in the cortex. In very deep insulin hypoglycemia there were no responses either to pain or visual stimulation.

UNIDIRECTIONAL TRANSPORTS OF CERTAIN SUBSTANCES IN DOG INTESTINE. B. E. Vaughan*, E. M. Jacobsen* and E. L. Alpen. U. S. Naval Radiological Defense Lab., San Francisco, Calif.

The constant perfusion technic in Thiry-Vella loops has been developed to examine functional behavior of dog jejunum and ileum. Loop blood supply was

left intact, and preparations remained normal after 6 months. Net and unidirectional sodium transport were investigated by Goldman's procedure (Fed. Proc. 15:78, 1956), using Na^{22} label. In such "transfer-in" experiments, the perfusates were buffered solutions which were multiply isoionic with respect to plasma. Immediately following transfer-in experiments, net and unidirectional reverse transport were determined by separate, "transfer-out," experiments, in which perfusates containing no label were circulated 1 hr after intravascular injection of additional isotope. Sodium ion concentration was varied in perfusates and plasma, in the latter by dehydrating the animal. Under the chosen experimental conditions, kinetic behavior of the label can be defined simply by a constant time rate of change. The transfer coefficients, so determined are found to be independent of sodium concentration and concentration gradient. Net transfer by chemical assay and by unidirectional transfers in transfer-in and transfer-out experiments agree closely. Sodium transfer is unchanged in magnitude when transport is against the concentration gradient, where the gradient is represented by concentrations of 180 mEq/l. in plasma and 100 mEq/l. in loop. Thus, unlike a diffusion system, observed sodium transport requires metabolic energy expenditure. Analogous experiments using H^3 labelled water and C^{14} labelled urea were performed; however, isotope behavior in water and urea systems cannot be defined as simply as in the case of sodium. Studies are in progress on the additional parameters necessary for the determination of transfer coefficients for these substances.

PEAK URINARY EXCRETION OF 5-HYDROXYINDOLEACETIC ACID FOLLOWING AROUSAL IN HUMAN BEINGS. George L. Wadsworth*, Franz Halberg, Paul Albrecht* and George Skaff*. Cambridge State School and Hosp. and Univ. of Minnesota Med. School, Minneapolis.

In the mouse, a daily drop in the 5-hydroxytryptamine (5-HT) content of brain usually precedes the time of initiation of peak bodily activity (Proc. Soc. Exper. Biol. & Med. 92:703, 1956). Possibly related changes in the excretion of urinary 5-hydroxyindoleacetic acid (5-HIAA) are reported herein for human beings. Samples of urine were collected from 9 institutionalized patients, at 3-hr intervals over a 27-hr period. At these intervals, rectal temperatures also were measured and the occurrence of a temperature rhythm was ascertained for these subjects. Urinary 5-HIAA content was determined by the method of Udenfriend et al. (J. Biol. Chem. 216:499, 1955). The patterns of excretion of 5-HIAA from one 3-hourly period to the next were quite variable in these subjects but they were not entirely random. The mean change for the group showed a peak excretion during the period from 6 a.m. to 9 a.m., the 5-HIAA content during this period being on the average about 60% higher than during the rest of the day. The finding of peak excretion of 5-HIAA following arousal, in conjunction with results of earlier work, is in keeping with the assertion that changes in 5-HT constitute an aspect of arousal in human beings.

FUNCTIONAL AND STRUCTURAL CHANGES INDUCED IN SKELETAL MUSCLE BY SEVERE POTASSIUM DEFICIENCY. Khalil G. Wakim and W. Newlon Tauxe*. Sections of Physiology and Clin. Pathology, Mayo Clinic and Mayo Fndn., Rochester, Minn.

Weanling albino rats of the same age (weight, 37 to 45 gm.) were divided into 3 groups. For 3 wk group 1 was fed the regular kennel ration; group 2, a synthetic K-free diet, and group 3, a synthetic diet with the required potassium added. At the end of the period the total body weight, the work output, endurance and histologic structure of the gastrocnemius muscle group were studied and compared. The animals on kennel ration tripled their body weight (av. 125 gm). Those on synthetic K-free diet had an average body weight of 52 gm, while those on synthetic diet with potassium added averaged 71 gm. The work output of the gastrocnemius muscle group of animals on kennel ration averaged 35 gm meters/100 sec, while those on synthetic ration averaged 4 gm meters, and those on synthetic ration with potassium added averaged 15 gm meters. The histologic picture of the gastrocnemius muscle of the animals on the

potassium-free diet was characterized by marked reduction in size of the muscle fibers, so that the nuclei appeared more numerous. Both the nuclei and the nucleoli were enlarged. The muscles appeared pale and the fibers had undergone fibrillary degeneration and did not stain uniformly. The cross-striations were somewhat irregular. Addition of potassium to the synthetic diet for 2 wk led to a return of the histologic picture of muscles toward normal status. No signs of inflammatory reaction were noted.

CORRELATION OF INTERVAL OF FIXED COUPLING WITH CONSTANT CURRENT AT THE CATHODE AND AT THE ANODE IN THE DOG VENTRICLE. Sheppard M. Walker and Ann Baxter*. Univ. of Louisville School of Medicine, Louisville, Ky.

Male mongrel dogs were anesthetized with 275 mg/kg of sodium barbital and prepared for artifical respiration. The heart was exposed in these animals and 1 stimulating electrode was placed under the epicardium midway between the base and the apex of the left ventricle. The other stimulating electrode was placed in the right hind paw. Electrocardiograms were obtained with a Grass Model III D electroencephalograph. Constant current for stimulation was supplied from a 65-volt battery. When the electrode on the ventricle is the cathode, 0.2-0.8 ma of constant current is required to induce ectopic ventricular beats. Under these conditions the ectopic ventricular beats occur near the P wave in the cardiac cycle, the interval of fixed coupling between the ectopic beat and the preceding normal beat being about 0.35 sec. When the electrode on the ventricle is the anode, 1 to 1.7 ma of constant current are required to induce ectopic ventricular beats. Under these conditions the ectopic ventricular beats usually occur at the end of the T wave, the interval of fixed coupling between the ectopic beat and the preceding normal beat being about 0.23 sec. It is suggested that changes in rate of repolarization induced at the stimulating electrode by the constant current may determine the time in the cardiac cycle when the ectopic ventricular beat is initiated. (Supported in part by grant H-697(C7) from the Natl. Heart Inst., USPHS.)

CLINICAL METHOD FOR MEASUREMENT OF RESPIRATORY ELASTANCE, RESISTANCE, MAXIMAL PRESSURES AND VOLUMES. Harry J. Wander*, John J. Connolly, Jr.*, Patrick S. O'Halloran*, and Alfred W. Brody. Creighton Memorial-St. Joseph's Hosp., and Creighton Univ. Med. School, Omaha, Nebr.

The patient breathes through a mouthpiece with a laterally connected pressure meter, into a flowmeter attached to a 3-way stopcock. Maximal pressures are obtained at end tidal volume with the stopcock closed. Respiratory volumes are obtained by integration of the flow, or from an attached spirometer. Elastance is obtained by inflating the voluntarily relaxed patient with a constant gas flow through the stopcock sidearm, and dividing the rate of pressure increase at the mouth by the rate of volume increase. Satisfactory passive deflations may be analyzed for k_1 and k_2; however it is much easier for technicians to make and read records for resistance is sinusoidal pressure and volume oscillations are produced at about 10 cps (J. Appl. Physiol. 8:587, 1956). As a result of this study, we suggest a maximal flow during such oscillations of about 1 l/sec. This flow stabilized the measured resistance despite changes in the ratio of k_1 to k_2 (in normals). Resistance is the measured ratio of peak pressure to peak flow. Records for all the procedures are made and read by a technician in about 1-1/2 hr. Intubation is not required. (Supported (in part) by research grant H-1951 from Natl. Heart Inst., USPHS.)

RENAL FLOW OF OLIGOCYTHEMIC BLOOD CONTAINING HEMOGLOBIN AS A FUNCTION OF ARTERIAL PRESSURE. William H. Waugh (intr. by William F. Hamilton). Dept. of Physiology, Med. College of Georgia, Augusta.

Kinter and Pappenheimer (Am. J. Physiol. 185:399, 1956) believe that plasma skimming is the basis for renal autoregulation of blood flow which they did not

observe at very low arterial hematocrits. To assure a much higher oxygen content of erythrocyte deficient blood supplying the kidney, oligocythemic blood containing large amounts of free hemoglobin was employed in the following study of renal flow. Hematocrits of pentobarbitalized dogs were lowered by rapid graded bleedings of 1-2% of body weight and transfusion of most of the autogenous blood after it had been hemolyzed in 2 volumes of water, the stroma removed by centrifugation, and sodium chloride added to render the supernatant isotonic. Hypertension was then produced by bilateral section of the vago-depressor trunks and occlusion of the carotid arteries. Single kidneys of normal dogs were rapidly transplanted to a femoral artery of the oligocythemic hypertensive dogs. Arterial pressure of the transplanted kidney was varied locally and its blood flow measured directly. Arterial hematocrits were less than 15% and renal blood flow rates were frequently greater than normal. However, flows remained relatively constant despite large variations in perfusion pressure and the intrarenal venous pressure, measured by catheterization, remained relatively low. Thus, the near constancy of blood flow with variable arterial pressures in the isolated kidney perfused by the neurogenically hypertensive dog does not appear to be dependent upon the presence of erythrocytes or upon a variable resistance in the distal intrarenal veins. (Supported by Grant HTS 5044, Natl. Heart Inst., USPHS.)

EFFECTS OF STIMULUS STRENGTH ON CONTRACTIONS OF ISOLATED HEART MUSCLE. William J. Whalen (intr. by Victor E. Hall). Dept. of Physiology, Univ. of California School of Medicine, Los Angeles.

The excised cat papillary muscle in physiological saline was stimulated repetitively by mass electrodes. Abruptly increasing the threshold voltage by a factor of two or more was followed after a short delay by a gradual increase in contraction strength, which in some instances exceeded 100%. This suggested that some fibers, quiescent at the lower voltage, were activated by the stronger stimulation. "Treppe" of the recruited fibers might account for the delay in the onset of the response. However, after recording resting and action potentials from more than 300 single cells from 6 papillaries, no inactive fibers have been found when stimulating at threshold voltage so that, while the search is continuing, the hypothesis seems doubtful. Results from the cat atria under similar conditions suggest an alternative hypothesis, namely, stimulation of autonomic nerve endings. With the cat atria, doubling the threshold voltage causes first a marked fall in the contraction strength, then a return to the control level or occasionally above it. Atropine abolishes the dip and unmasks or accentuates the rise. Dihydroergotamine does not appreciably block the rise, but Xylocaine appears to modify the responses significantly. These observations make it fairly certain that the dip is due to the release of acetylcholine with strong stimulation and it is conceivable that the rise may result from release of epinephrine or nor-epinephrine. Work in progress will test these suggestions and their applicability to the cat papillary as well as the possibility that one of the catechol amines may be the "post-stimulation" substance (Rosin and Farah, Am. J. Physiol. 180:75, 1955).

PROPERTIES OF CRYSTALLINE Δ PROTEIN. John I. White and Sylvia Himmelfarb (intr. by William R. Amberson). Dept. of Physiology, Univ. of Maryland School of Medicine, Baltimore.

In papers from this laboratory (Am. J. Physiol. 188:205, 1957) the preparation and properties of Δ protein and the combination of Δ protein with myosin to form the complex, Δ-myosin, have been described. Recently, Δ protein preparations have been crystallized by dialysis against 0.01 M acetate buffer, pH 5.4, containing 16 gm/l. $(NH_4)_2SO_4$. Crystallization begins when the pH falls to 5.5 and is complete at pH 5.4. Two highly bire-fringent crystalline forms have been observed, one consisting of hexagonal platelets and the other of rectangular prisms, which resemble the crystalline form of carp nucleotropomyosin. Crystals are readily obtained also from Δ protein prepared by extracting washed rabbit muscle with HCl at pH 2.0, neutralizing, and precipitating Δ protein from the

neutralized supernatant solution by adjusting pH to 4.8. Twice crystallized Δ protein had an S_{20} of 4.8 and showed a somewhat enhanced ability to complex with myosin to form Δ-myosin, as demonstrated in electrophoresis and in the synthetic boundary cell in the ultracentrifuge. The intrinsic viscosity increased from a precrystallization value of 1.27 to a value of 3.00 after crystallization. Determination of UV absorption at 260 mμ after separation of nucleic acid from the protein by the Schneider method revealed only trace amounts of nucleic acid. While Δ protein resembles nucleotropomyosin in crystal structure, it may be differentiated from nucleotropomyosin by the absence of nucleic acid.

EFFECT OF PERCHLORATE ON URINARY EXCRETION OF RADIOIODIDE, CREATININE AND CHLORIDE. R. R. Widner, L. T. King, A. C. Hass and N. S. Halmi (intr. by R. G. Janes). Dept. of Anatomy, State Univ. of Iowa, Iowa City.

Comparisons were made between rats injected with 2 ml/100 gm of sodium perchlorate (154 mEq/l.) or the same amount of water. All rats were given 12 mg of propylthiouracil and a tracer dose of radioiodide. Determinations were made on the urine excreted between 1 and 5 hr after the injection of radioiodide. Blood was taken either before and after or only after the period of urine collection. In the perchlorate treated rats a) radioiodide excretion was significantly enhanced, especially if urine flow was low, as in the rats which were bled before the collection of urine; b) clearance of endogenous creatinine was not affected; c) clearance of chloride was increased, but it was estimated that over 99% of filtered chloride was still reabsorbed. Perchlorate does not appear to affect glomerular filtration and prevents the tubular reabsorption of a much greater percentage of filtered radioiodide than of filtered chloride. (Supported by grant A-932, USPHS.)

ROLE OF THE NEURAL AND HORMONAL COMPONENTS OF THE SYMPATHETICO-ADRENAL MEDULLARY SYSTEM IN THE BLOOD PRESSURE AND PULSE CHANGES DURING FASTING AND REALIMENTATION WITH HIGH CARBOHYDRATE DIETS. C. M. Wilhelmj, William Pettinger* and H. H. McCarthy*. Depts. of Physiology-Pharmacology and Surgery, Creighton Univ. School of Medicine, Omaha, Nebr.

When normal dogs are fasted the blood pressure and pulse rate decline to low levels. Realimentation with high carbohydrate diets fed at a level of 120 cal/M^2/hr causes the systolic pressure and pulse to rise significantly above the fasting and control values while the diastolic remains low. Dogs with bilateral paravertebral ganglionectomy and denervation of the adrenal glands show a fall of pulse rate but not the fall of blood pressure during fasting (a tendency to rise is common). Following realimentation with high carbohydrate diets, the blood pressure does not rise above the fasting level nor the pulse above the control level. In these preparations both the hormonal and neural components have been removed. Which is responsible for the difference from normal dogs? In 4 dogs, 1 adrenal was removed and the other denervated. These preparations showed a fall of systolic pressure and heart rate during fasting and a rise above the fasting values during realimentation with high carbohydrate diets similar to normal dogs. It thus appears that the neural component is primarily responsible for the cardiovascular responses during fasting and realimentation with high carbohydrate diets. (Aided by American Heart Assoc. and Natl. Heart Inst., USPHS.)

CARBON MONOXIDE IN PLANTS. S. S. Wilks (intr. by Hans G. Clamann). Dept. of Physiology-Biophysics, School of Aviation Medicine, USAF, Randolph AFB, Texas.

A method for detecting and quantitating carbon monoxide in animal tissues has been applied to green plants. The method has demonstrated the presence of CO in the green structures of a variety of plants. The CO content of alfalfa leaves has been found to be of the order of 2 ml/100 gm. It has been further demonstrated that chlorophyllaceous structures, confined in light transparent

gas-tight compartments, and exposed to sunlight in the presence of oxygen and water, liberate carbon monoxide. The phenomenon will not occur in the absence of light, water or oxygen. Dry, powdered leafy vegetation in the presence of O_2, H_2O, and light has been found to liberate CO. Sterilization of the hydrated leaf powder in absence of oxygen will not inhibit this formation of CO when the sterilized medium, in the presence of O_2 and H_2O, is exposed to light. Addition of chlorophyll extract will augment the formation of the CO. Exposure of hydrated leaf powder to direct sunlight for 30-40 hr will yield CO in the order of 1 ml/gm.

RESPONSES OF RATS TO HYPOTHERMIC CARDIAC ARREST. P. Willard* and Steven M. Horvath. Dept. of Physiology and Cardio-vascular Lab., State Univ. of Iowa, Iowa City.

Studies were made to determine the feasibility of inducing by hypothermic procedures prolonged cardiac arrest with subsequent resuscitation. The following procedure was employed on 18 rats. The rats were subjected to hypercapnia, anoxia and cold followed by immersion in an ice bath in which their colonic temperatures were reduced to an average of 1.3°C. Immediately upon immersion in the ice bath electrocardiograms and a variety of body temperature measurements were taken. In all cases the P waves had disappeared before the rats were immersed in the ice bath and the heart beat became progressively more idioventricular as the cooling proceeded. Electrical activity from the heart was no longer evident when the colonic temperature reached an average of 4.1°C (S.D. ±3.0°C). Cardiac arrest was maintained for an average of 43 min. On rewarming electrical activity became evident again at an average colonic temperature of 7.6°C (S.D. ±3.8°C). An exponential relationship was found between the heart rate and colonic temperature both during the cooling and rewarming phases. All of the animals recovered cardiac activity and of the 7 animals surviving for more than 24 hr, 5 lived for many months.

EFFECTS OF EXTRACTS OF FOETAL WHALE THYMUS GLANDS ON SKELETAL MUSCLE. H. Wilson, P. T. Nowell, A. Wilson (intr. by H. M. Hines). Dept. of Pharmacology and General Therapeutics, The Univ., Liverpool, England.

Foetal whale thymus glands have been extracted with acetone by the method previously described (Am. J. Med. 19:697, 1955). When freed from acetone the extract was passed through ion exchange resin Amberlite IRC '50.' Elution by 0.2 M. K_2HPO_4 produced a fraction which formed a precipitate with ammonium reineckate. The resultant reineckate complex yielded a chloride (product R). The effects of product R and the acetone extract from which it was prepared have been observed on skeletal muscle. Small doses of product R potentiated the response of the frog rectus muscle to acetylcholine and increased the twitch height of the cat tibialis anterior muscle in response to stimulation of its nerve. Larger doses produced in the cat contracture followed by a depression of the muscle twitch height, from which the preparation slowly recovered. The effects were similar to those reported with acetone extracts of foetal whale thymus glands. They were not produced by extracts of lymph nodes or voluntary muscle and were not due to the electrolyte content of the thymus extracts. (Aided in part by a grant from the United Liverpool Hosps. Med. Research Fund, England.)

EFFECTS OF REPETITIVE ACTIVATION ON GROUP I ACTIVITY. Victor J. Wilson. Rockefeller Inst., New York City.

Monosynaptic reflex transmission, facilitation of synergists, inhibition of antagonists within a myotatic unit and disynaptic inhibition, were studied in spinal cats with respect to early post-tetanic potentiation and low-frequency depression. These group I functions are all enhanced following a brief high-frequency tetanus (early potentiation). To explore low-frequency depression of inhibition and facilitation 0.1/sec was used as control frequency. Conditioning stimulus frequency was then raised, test stimulus frequency remaining at 0.1/sec, the two being adjusted so that the conditioning-test interval remained

fixed throughout. In this way the test system could be maintained constant and the effect of frequency variation on facilitatory or inhibitory power of conditioning volleys could be measured. Homosynaptic transmission always exhibits low-frequency depression. Facilitation is usually more depressed when conditioning and testing volleys are nearly simultaneous than when they are separated by 1 - 1.5 msec. This indicates that early events, responsible for homonymous and heteronymous transmission, are more sensitive to low-frequency depression than is residual facilitation. Direct inhibition does not suffer low-frequency depression (confirming Beswick and Evanson, 1957) whereas disynaptic inhibition (flexor longus digitorum-gastrocnemius) often does. Inhibitory junctions being insensitive to low-frequency depression, depression of disynaptic inhibition appears due to properties of the primary relay from afferent fibers to interneurons in this pathway. That direct inhibition can be potentiated shows it to be sufficiently labile that decreases in efficiency at inhibitory junctions during repetitive activity should be revealed. Homosynaptic transmission is more sensitive to events concurrent with and following repetitive activation than are other aspects of action by group I fibers.

INFLUENCE OF EXERCISE AND TESTOSTERONE PROPIONATE ON THE COMB RESPONSE AND BODY WEIGHT OF CHOLESTEROL FED CAPONS. Harry Y. C. Wong, Abbie Wong*, Joseph Anderson*, Tatsuo Kimura* and Frank B. Johnson*. Dept. of Physiology, College of Medicine, Howard Univ. and Armed Forces Inst. of Pathology, Washington, D. C.

It has been previously reported by our laboratory (Am. J. Physiol., 178:269, 1954) that standardized exercise has a depressant effect on the comb response of capons treated with 1.0 mg of testosterone propionate daily for 10 days. The following experiment was undertaken to study the effects of exercise and testosterone propionate on the comb response and body weights of cholesterol fed capons for an extended period of study. Six groups of capons were studied: 1) controls on plain mash without therapy; 2) controls on plain mash but exercised; 3) cholesterol-fed only; 4) cholesterol-fed and exercised; 5) cholesterol-fed capons treated with testosterone propionate; and 6) cholesterol-fed capons treated with testosterone propionate and exercised twice daily for 30 min. At the end of 11 wk of treatment, it was noted that there were no significant differences in comb size between groups 1, 2, 3, 4. However, there was a marked difference between groups 5 and 6 when compared to the other groups. In addition, the comb size of group 6 was much smaller than that of group 5. The body weight of the various groups was much less than the controls on plain mash without therapy. The foregoing data suggest that exercise has a profound effect on the comb growth of androgen-treated capons placed on a cholesterol diet. Also it seems that exercise or testosterone propionate reduced the body weights of the chicks when compared to the untreated controls on plain mash. (Supported in part by grants from the Natl. Heart Inst., USPHS., Washington Heart Assoc., and Committee on Research, AMA.)

NERVE TERMINATIONS IN THE VENTRAL COCHLEAR NUCLEUS. Paul A. Young*, Margaret M. Powers* and George Clark. Depts. of Anatomy and Physiology, Univ. of Buffalo, Buffalo, N. Y.

The various stains for nerve endings are characterized mainly by their capriciousness. With a silver method we have recently developed, there is apparently some order in this capriciousness. With this method boutons are occasionally stained throughout the anterior horns of the spinal cord, rarely in the posterior horns of the spinal cord, in the vestibular nuclei, reticular formation of the medulla, etc. We have never found impregnated endings in the nucleus gracilis and nucleus cuneatus. In marked contrast the endings around the cells in the ventral cochlear nucleus are well stained. Each cell is virtually covered with these impregnated boutons. This routine finding suggests that the capriciousness of the stain may well be more apparent than real and that it may lie in chemical differences in the endings.

DISAPPEARANCE OF BACILLUS MEGATHERIUM BACTERIOPHAGE FROM CIRCULATION OF THE DOG. Marvin L. Zatzman and Robert Keller (intr. by James E. Randall). Depts. of Physiology and Pharmacology and of Microbiology, Univ. of Missouri Med. Ctr., Columbia.

The results of a study of the biological interrelationships of virus particles in a mammalian host are reported. A bacterial virus was chosen for study because: 1) it is a non-multiplying system in the animal host; 2) its size is in the range of animal viruses; and 3) quantitative assay methods for bacterial viruses are well established. Single 10 ml injections of a broth suspension containing approximately 10^9 B. megatherium bacteriophage particles per ml were introduced via the femoral vein of anesthetized dogs. Blood samples were obtained from the cannulated femoral artery of the opposite limb at short-time intervals. In some animals the right ureter was catheterized and urine samples were collected at 10- or 20-min intervals. Approximately 5-gram samples of kidney, spleen and liver were homogenized for assay. The number of bacteriophage particles in each of the blood, urine and organ samples was determined by a standard pour-plate method. Disappearance curves of the phage particles from the plasma of arterial blood show a double exponential decrease with time. There are apparently several methods by which the animal eliminates bacteriophage from the circulation. Among these are: 1) a non-specific "antibody" system; 2) diffusion of particles to the interstitial fluids; 3) "filtration" of viable particles by organs such as the liver and spleen; and 4) excretion with the urine. (Supported in part by USPHS Grant E-752.)

DRUGS AFFECTING BULBOCAPNINE CATATONIA. Gerhard Zetler (intr. by Williamina A. Himwich). Pharmacological Inst., Univ. of Kiel (Germany), and Galesburg State Research Hosp., Galesburg, Ill.

The "catatonic" effect of bulbocapnine was measured quantitatively in mice by their ability to climb a vertical rod. Under the influence of bulbocapnine the mice remain motionless on the rod, and the duration of this effect is proportional to the dose of bulbocapnine. Previous results disclosed that for the dose-range of 30-70 mg/kg bulbocapnine injected subcutaneously the log dose-response line obeyed the equation $Y = 18.6\ X - 23.8$ and the index of precision λ was 0.135. The following substances which antagonized the tremor-producing effect of harmine (Zetler: Arch. exper. Path. u. Pharmakol, in press) had no influence on bulbocapnine "catatonia": Apomorphine, atropine, scopolamine, belladonnine, benzhexol (Artane), caramiphen (Parpanit), cycrimine (Pagitane), Akineton, Soventol, adiphenine (Trasentine), Covatin, mephenesine, promethazine, thiazinamium, ethopropazine, diethazine, phenytoin, LSD-25, 5-hydroxytryptamine, tryptamine, indole and urethane. Morphine and harmine were also ineffective. Only amphetamine (3.6), ephedrine (23), Benadryl (6.3) and the Benadryl derivatives, Disipal (10.2) and Rigidyl (20.3), were potent bulbocapnine antagonists (the figures in parentheses are the intraperitoneal doses protecting 50% of the animals against 50 mg/kg bulbocapnine subcutaneously). Cocaine and mescaline had a very weak antagonistic potency, shown only in their low dosage range. Bulbocapnine "catatonia" was enhanced after chlorpromazine, Hydergine and reserpine. Reserpine alone produced a "catatonic" state similar to that of bulbocapnine whereas chlorpromazine and Hydergine alone did not modify the ability of mice to climb the rod. Only Benadryl, Disipal and Rigidyl antagonized both bulbocapnine "catatonia" and the harmine-induced tremor.